Archives of Dermatology and Syphilology

VOLUME 21 FEBRUARY, 1930 NUMBER 2

THE PRESENT DAY TENDENCY OF DERMATOLOGY*

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This, the fifty second annual meeting of the American Dermatological Association is marked by several auspicious circumstances. Our farthest point west until now was reached seventeen years ago, when we for the first time crossed the Mississippi and met at St. Louis. Now we have crossed the continent and, like the old Greeks, joyfully acclaim the western sea. May we not believe that this is another evidence of the constantly accelerated march of dermatologic science, and that the leagues we have covered and the fields we have won are but an earnest of new quests to be pursued and of regions as yet unknown to be explored?

Another noteworthy matter is the issuing of a presessional volume which, while so far spoken of as an experiment, has already proved its worth in other similar bodies. I believe that it will be continued in this association, and that its effect will be to improve materially the character and value of our discussions.

Not the least of the features which make this a memorable occasion is the presence of the renowned master of our art who has crossed the ocean and the full width of our land to be with us today. In the name of the association, as well as in my own, I express to him our appreciation, our pleasure and our grateful thanks.

On such an occasion one is tempted to look forward and to indulge in a little speculation as to what the future has in store for dermatology, and as to the direction in which we shall travel for the next few years. Since the future can be read only in the light of the past, we needs must first pause for a brief moment and glance back over the road already trod.

Dermatology, like all other sciences, began with a recognition and naming of the forms and species which are the objects of its study. The next obligatory step was the seeking after the relationships existing between them, their grouping or classification. Those who essayed such arrangement by the insufficient light of dawn constructed artificial orders and genera, a fault which persists today in the measure commensurate with our ignorance. Then came the anatomic period,

* Submitted for publication, Aug. 15, 1929.

* Address of the President read at the Fifty-Second Annual Meeting of the American Dermatological Association, San Francisco and Del Monte, July 2, 1929.

devoted to the study of the structural elements of which the objective phenomena are built and their arrangement. Its natural result was to divert attention from the subject of the disease to the lesion. The laborers in this field did their work so well that today it is only necessary to glean after the reapers and to pursue certain refinements here and there. Then came a time in which knowledge was again mightily advanced, and in which we still live, which dealt largely with the exogenous causes of disease. The word etiology in many instances acquired a new meaning, and the old idea of disease arising from noxa outside the body was clarified, illustrated and made precise.

As every great advance in knowledge tends to minimize or even at times to make us forget our older information, so here some seemed to feel as though the discovery of the specific organism told us all that we needed to know about a disease. We have now arrived at a more correct estimate of relative values, and while we will not return to the old notions about temperaments and humors, we look on the reactions of the cell as influenced by a variety of internal factors on which our attention is now chiefly centered.

Our present attitude has been made possible by the astonishing developments of chemistry in the last quarter of a century, which have made its language unintelligible to those who, so to speak, have straggled behind the column. These developments have on the one hand erased the frontier between that science and physics, and on the other pushed far into the realm of biology. The recognition of the colloidal state of matter leading to the conception of the living cell as a unit colloid mass is a striking instance of the confluence of physics, chemistry and biology. The contributions of biochemistry and of biophysics are today uppermost in the mind of the biologist and are growing day by day. The determination of the hydrogen ion concentration of body fluids has led to the wonderfully delicate investigation of the p_H of the living cell, with its promise of new developments in the field of dermatology. How much that was mysterious has been illumined by the revelation of the endocrines, hormones and vitamins! The discovery of ergosterol, of the relations existing between epinephrine and melanin, accounting for the symptoms of Addison's disease, the work of Bloch with the primrose, and of Werner Jadassohn with *Ascaris*, establishing the production of allergy by nonproteins, Wile's work with lipids in xanthoma, and Klauder and Brown's work on the calcium-potassium relation in cutaneous irritability, are a few random illustrations of the growing importance of biochemistry. I believe that Burrow's researches into the biochemical aspects of cancer will throw a ray of light into this dark corner of pathology.

A necessary consequence of our broadened knowledge is to make us look on diseases not as entities, but as incidents in the greater biology

which embraces all the phenomena of life. As some one has said, to maintain a distinction between physiology and pathology is like dividing meteorology into a science of good weather and a science of bad weather. The distinction between the normal and the abnormal is largely a matter of the point of view. We think it normal to eat a sheep but abnormal to be eaten by a tiger. The distinction is unscientific, albeit at times useful.

The larger conception of medicine as a part of biology opens new avenues of approach to many of our problems. A review of the changes in the meaning of the word "eczema" illustrates this shifting of the angle of observation. The older definitions were limited to the moist forms. Later, a clearer clinical insight, aided by histologic studies, showed the oneness of this type or stage with others that had until then borne other names. Then for a time there was a search for one or more micro-organisms as necessary causes. So far our mental processes in this regard were inhibited by the conception of eczema as an entity. A recognition of the fact that a variety of external agents may determine phenomena in no way distinguishable from those of presumably internal origin has changed the meaning of the word eczema to signify a certain type or mode of reaction of the skin; in other words, a symptom. The word will probably fall into disuse, or if it survives will be applied not to the local phenomenon but to designate chronic biochemical imbalance, in many instances at least, as Schamberg has shown, consisting of an excess of uric acid in the blood, manifesting itself by increased epithelial permeability.

In like manner conceptions of other diseases grow and change with better understanding, from the phenomena produced to the wider condition of which they are only a part.

One consequence of the larger outlook is to make us dermatologists realize that some of the distinctions we make between disease forms are based rather on our approach to them than on their true nature. We recognize families and genera among dermatoses, which means that they are related, and relation means community of origin. We must have names for the things we deal with, but we must remember that names do not always stand for real things. In some instances we are perhaps using a number of names to describe different phases of one process, readily seen to be such when viewed from a biologic standpoint.

It seems, therefore, that for the present and for some time to come the new knowledge in medicine is to come from the quarter of biophysics and biochemistry, and that dermatology, because it is one of the younger members of the family of medical sciences, may be expected to make even longer strides than the others; in a word, that in the future dermatologists will become more and more biologically minded.

THE SENSITIZATION OF THE SKIN TO MESOTAN*

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In spite of the fact that the conception of hypersensitivity of the skin has been current for more than thirty years, it is only comparatively recently that workers have been able to reproduce this condition experimentally by the external application of substances with a known chemical composition. Such work as has been reported in this field will be described in detail at the end of this paper.

In 1902 a new drug, mesotan, was put on the market for percutaneous treatment in those conditions which respond to salicylates. A considerable literature on this substance appeared in the next few years. From the start, it was noted that in certain concentrations and under certain conditions of application the drug caused eruptions of the skin; in all but one case cited, the eruptions did not occur after the first, but only after repeated, applications. Among the many writers [1] who reported on conditions of the skin from the use of this drug, Kayser [2] spoke of having noticed a true sensitization. He said, "for if the condition has reached the stage of vesiculation, a hypersensitivity of the whole skin, lasting usually for months, results."

The following experiment deals with an attempt to sensitize the skin of persons to mesotan by percutaneous applications and to study the resulting hypersensitivity. Mesotan,[3] the methoxymethyl ester of salicylic acid $\left(C_6H_4<^{OH}_{COOH_2-O-CH_3}\right)$, is formed by the action of formaldehyde, methyl alcohol and hydrochloric acid on sodium salicylate. It is a white or yellow liquid with a faint odor suggesting

* Submitted for publication, July 31, 1929.

* From the Skin Clinic, University of Breslau, Geheimrat Prof. Dr. J. Jadassohn, Director.

1. Floret, T.: Deutsche med. Wchnschr. **28**:765 (Oct.) 1902. Ruhemann, J.: Deutsche med. Wchnschr. **29**:23 (Jan.) 1903. Kayser: München. med. Wchnschr., 1903, no. 38, p. 1627. Sembritzki: Deutsche med. Wchnschr. **29**:999 (Dec.) 1903. Kropil, J.: Wien. med. Presse **44**:611 (March) 1903. Liepelt, K.: Berl. klin. Wchnschr. **40**:361 (April) 1903. Strass, A.: Wien. klin. Rundschau **18**:905 (Dec.) 1903. Gröber, A.: Die Heilkunde **2**:5 (Feb.) 1903. Zeigan, F.: Berl. klin. Wchnschr. **40**:279 (March) 1903. Frankenburger, A.: München. med. Wchnschr. **50**:1297 (July) 1903. Berliner, C.: Monatsh. f. prakt. Dermat., 1904, vol. 38. Sack, A.: Monatsh. f. prakt. Dermat., 1904, vol. 38. Korach: München. med. Wchnschr., 1904, p. 1516. Wills, J. P.: Monatsh. f. prakt. Dermat. **41**:287 (Sept.) 1905.

2. Kayser (footnote 1, reference 3).

3. Heffter: Berlin, Julius Springer, 1923, vol. 1, p. 1001.

wintergreen. It has a low solubility in water (0.019 per cent). It is easily split; after a short contact, water alone causes a small degree of splitting into free salicylic acid and formaldehyde. Unsplit mesotan is absorbed by the skin and appears split in the urine up to 8 per cent.

The experiment was divided into four sections: 1. A preliminary study was made to see in what proportion of cases, if in any, a primary hypersensitivity to the drug was to be found. 2. An attempt was made (experiments 1 to 4) to sensitize four groups of human beings to the drug by the percutaneous route, under varying modes of application. 3. A study of the resulting hypersensitivity (experiments 5 to 7) for monovalency or polyvalency, for the presence or absence of an urticarial element and for passive transference was made. 4. The effort was made (experiment 8) to sensitize the skin of guinea-pigs and rabbits by percutaneous applications.

EXPERIMENTAL WORK

Preliminary Tests.—During a period of two months all of the patients on the women's ward, numbering 124, were tested with 10 per cent mesotan in olive oil or vaseline by eczema skin tests,[4] and none was found to be hypersensitive; that is, none gave the ++ reaction.[5] The tests were performed by putting the substance on a piece of lint about 0.5 cm. square, applying this to the skin and covering it with a 1.5 cm. square of cellophane and a piece of plaster (bonnaplast), 5 cm. in diameter. The tests were read after twenty-four hours.

Thirty-two of the patients were given eczema skin tests with concentrations of mesotan varying from 5 to 100 per cent, but no marked differences to the varying concentrations were found (reactions described as +[6] sometimes occurred, but there were no ++ reactions), nor was it noticed that it made a visible difference whether vaseline or oil was used as the vehicle. However, two interesting cases (A and B) of hypersensitivity developed during the course of these tests.

Case A.—In a woman, aged 18, whose case was diagnosed as uncomplicated gonorrhea, eczema skin tests gave the results shown in table 1.

Whereas the patient reacted negatively to 10 per cent mesotan in the middle of December, she gave a strong positive reaction to the same test about one month later, after having been brought in contact with the drug only through minute quantities applied in eczema skin tests.

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4. In cases A and B no two tests were applied to the same area.

5. A reading of ++ indicates a strong positive reaction with erythema and infiltration, in other words, a hypersensitivity. It is not possible to call this a true eczematous reaction because the infiltration is often too pronounced to warrant such a term, nor is it possible to class it with the urticarial reactions, because it does not develop and disappear quickly enough to be placed in this group; but when the hypersensitivity is very strong, papules and vesicles often appear; in other words, there is an epidermal reaction, and therefore I think I am right to classify the reaction tentatively in the eczematous group.

6. A + indicates a mild erythema without infiltration, or a reaction which is classed here as negative.

Case B.—In a woman, aged 22, the diagnosis was made of healing pyodermia of the leg. The results of eczema skin tests appear in table 2. It is seen that this patient was negative to 10 per cent mesotan on January 16, and seventeen days later, was strongly hypersensitive to the substance after application of only the minute quantities of the drug used in eczema skin tests. That the hypersensitivity in these two cases was monovalent will be shown later in the experiment.

Experiments 1 to 4.—Experiment 1: Of four patients (cases 1, 2, 3 and 4), all women, two had uncomplicated gonorrhea (cases 1 and 4), one had gonorrhea with adnexitis (case 3) and one had tertiary syphilis (case 2). These patients, who gave negative results at the start of the experiment to an eczema skin test with 10 per cent mesotan vaseline, were rubbed daily on the same area, approximately 5 cm. in diameter above the right elbow crease, for half a minute with 10 per cent mesotan vaseline; the area was then bandaged with a piece of gauze

Table 1.—*Results of Eczema Skin Tests with Mesotan in Case A*

Date	Mesotan, per Cent	Reaction
12/12/28 to 12/22/28	5	0
	10	0
	15	0
	20	+
1/15/29 to 1/16/29	40	+
1/16/29 to 1/17/29	50	+
1/23/29	Last two tests flared up spontaneously without new application of drug anywhere on body	
1/23/29 to 1/24/29	10	++

Table 2.—*Results of Eczema Skin Tests with Mesotan in Case B*

Date	Mesotan, per Cent	Reaction
1/15/29 to 1/16/29	10	0
	15	0
	20	0
	40	+
1/16/29 to 1/17/29	50	+
1/28/29 to 1/29/29	60	++
2/ 1/29 to 2/ 2/29	10	++

5 cm. in diameter, covered with 10 per cent mesotan vaseline, and with a strip of gauze bandage. The inunctions were started on Jan. 18, 1929. On February 6, as no hypersensitivity[7] had developed and as it was sought to increase the irritation from the drug if possible, the bandage was changed to a piece of lint 5 cm. in diameter, covered with 10 per cent mesotan vaseline, oiled silk and a gauze bandage. The inunctions were continued until the patient was discharged or until general hypersensitivity developed.

Local Reaction: Three (cases 1, 2 and 3) of the four patients developed a local reaction. The onset, which occurred between the twentieth and the twenty-fourth day of inunction, was gradual in two of the cases (1 and 2), but more sudden in the patient (case 3) who developed a general hypersensitivity. The type of reaction was an erythema with small papules; later, there was scaling

7. In these experiments hypersensitivity means a ++ reaction (marked erythema with infiltration) to an eczema skin test with 10 per cent mesotan vaseline. The test was applied on the forearm for hypersensitivity near the area of application (the arm), and on the back for general hypersensitivity.

during involution of the lesion. The fourth patient (case 4) received the inunctions for twenty-eight days without a local reaction and was then discharged. In both cases 3 and 4, the patient developed a mild erythema during the first days of inunction, which disappeared on the fifth day.

Hypersensitivity in an Area Adjacent to the Inunctions: The patient in case 1 gave a positive reaction to this test on the thirty-fourth day. A slight erythema had developed in the area of inunction on the twenty-second day, and had grown steadily more marked. In spite of this fact, the reaction to an eczema skin test on the right forearm had been negative on the twenty-ninth day; one may therefore conclude that the hypersensitivity in the area adjacent to the inunctions developed between the twenty-ninth and thirty-fourth day. On the thirty-fourth day the patient still gave a negative reaction to an eczema skin test on her back. Unfortunately, she could not be followed further, as she was discharged the next day.

The patient in case 3 began to develop a local reaction twenty-two days after the first application, but on the twenty-third day still gave a negative reaction on the right forearm and the back. On the twenty-fifth day the tests were repeated and were then found to give strongly positive reactions in both places. It is thus seen that two of the four patients developed hypersensitivity near the area of inunctions and that in one case this reaction was shown when general hypersensitivity was not present.

General Hypersensitivity: The patient in case 3, the only one of the series who could be observed until general hypersensitivity developed, first responded to the test on the twenty-fifth day; she had given a negative response to the test two days before. Although a marked positive reaction was first obtained at the same time on the right forearm and on the back, that on the back was obviously weaker than the reaction on the forearm.

The patients in cases 1, 2 and 4 had not developed general hypersensitivity on the thirty-fifth, thirty-second and twenty-ninth day, respectively, at the time when the inunctions were stopped and the patients were discharged.

Experiment 2: Three cases (5, 6, 7) were studied, all occurring in women. Case 5 was one of uncomplicated gonorrhea (?), case 6, small circinate psoriasis of face, and case 7, pernio (?).

These patients, who gave negative results at the start of the experiment to an eczema skin test with 10 per cent mesotan vaseline were rubbed daily on the same area, approximately 5 cm. in diameter, above the left elbow crease for half a minute with 100 per cent mesotan for from seven to nine days. Each day after the rubbing, the area was covered with a piece of lint 5 cm. in diameter, soaked in 100 per cent mesotan, and with oiled silk and a gauze bandage.

Local Reaction: All three patients developed a mild reaction in the elbow crease (erythema with a few small papules) between the second and fourth day. This remained unchanged until between the seventh and tenth day when there was a sudden marked increase in the severity of the local reaction, which now spread over and beyond the area of application, covering a site approximately 10 by 25 cm. in diameter. The reaction was papulo-erythematous in two of the cases (5 and 7), and papulovesiculo-erythematous in the third (6).

Hypersensitivity Near the Area of Application: In none of these three cases was a hypersensitivity shown to be present near the area of application before it developed at a distance.

General Hypersensitivity: Two of these patients (cases 6 and 7) developed general hypersensitivity. The patient in case 5 was obliged to leave the hospital on the ninth day, and although tested on the eighth day showed no general

hypersensitivity then. In case 6 the patient was shown to be generally hypersensitive on the eleventh day, three days after the marked local reaction commenced. She had given negative results to the test on the ninth day. On the eleventh day she also developed an erythematous area, 5 cm. in diameter, in the left axilla and on the left breast without any voluntary application of the drug there; however, these were areas to which minute quantities of the drug could easily have been carried by the motion of the arm or by the sleeve. In case 7 the patient was shown to be generally hypersensitive on the eleventh day. Skin tests applied on the ninth day gave negative results on the forearm and the back. On the eleventh day the patient had developed a positive reaction but of a peculiar nature. Tests were then reapplied and the reactions to these and all subsequent tests were so peculiar that they will be discussed in some detail. The test applied to the forearm on the eleventh day gave negative results when read after twenty-four hours; the one on the back produced one minute papule. After forty-eight hours both tested areas showed a mass of closely grouped papules which covered exactly the area on which the lint had lain, and in some spots were becoming confluent. The patient who had received the regular eczema skin tests given to all patients on admission to the hospital, had showed a negative reaction to all the tests except benzol; to this substance she had given a negative reaction after twenty-four hours, but a positive one after forty-eight hours. The differential diagnosis in this case lay between pernio and erythema induratum. When the patient was given a percutaneous skin test with tuberculin salve, the reaction was also delayed; it appeared after forty-eight hours, in the form of tiny papules which were closely grouped. The tests with 10 per cent mesotan vaseline were repeated several times; once she gave a mild positive reaction, but of the peculiar, sharply circumscribed, papular type, in twenty-four hours. The other times, the reaction appeared in from thirty-six to forty-eight hours and was always morphologically different from those of the other cases; it was papular in the early stages and sometimes later showed a circumscribed infiltration which was sharply limited to the actual area of application of the drug. What this difference in the time and character of the reaction means is not known. In his work with ursol, R. L. Mayer noted exactly the same characteristics in the reaction of some of his patients.[8] I have classed this patient among those considered generally hypersensitive, although the symptoms do not exactly correspond to the definition of hypersensitivity given. In this experiment, therefore, two patients became hypersensitive (cases 6 and 7), both on the eleventh day.

Experiment 3.—Of the three patients (cases 8, 9 and 10) tested, all women, one had uncomplicated gonorrhea (case 8), one secondary syphilis (case 9) and one uncomplicated gonorrhea (case 10).

These patients, who were negative at the start of the experiment to an eczema skin test with 10 per cent mesotan vaseline were rubbed in an area about 5 cm. in diameter, above the left elbow crease, with 100 per cent mesotan for one minute. This region was then covered with a piece of lint 5 cm. in diameter soaked in 100 per cent mesotan, and with cellophane and adhesive plaster (bonnaplast). The bandage was removed after twenty-four hours. Seven or eight days later, the same area was rubbed with sandpaper, care being taken to prevent bleeding, rubbed for one minute with 100 per cent mesotan and covered with a piece of lint soaked in 100 per cent mesotan, and with oiled silk and a gauze bandage for twenty-four hours. The type of bandage was changed on the second application because it was felt that the relatively strong reaction to the plaster, shown after

8. Mayer, R. L.: Personal communication to the author.

the first application, might obscure the nature of the reaction; the skin was rubbed with sandpaper to aid sensitization, as was done in the stimulating experiment of Bloch and Steiner-Wourlisch[9] on primula.[10] The sandpaper was used at the second although not at the first application, as the reaction to sandpapering followed by mesotan is so strong that a repetition after a short interval was thought inadvisable.

Local Reaction: In all three cases, there was a slight erythema of the bandaged area after the first application (without mechanical irritation). This erythema subsided in from one to four days. On removing the bandage after the second application (with mechanical irritation) there was found in all three cases a marked erythema with induration, sharply limited to the area to which the lint was applied. At the center of the inflammatory region there was a superficial yellow crust, from 2 to 3 cm. wide. In case 10 the local area remained unchanged for one day; the next day, the inflammation spread slightly, and forty-eight hours later, a strong inflammatory reaction had set in, which involved the whole circumference of the arm and extended 25 cm. above and 5 cm. below the elbow. The patient in case 8 showed only a small (1.0 cm.) increase in the erythematous area for one day; then the inflammation subsided gradually. The patient in case 9 was obliged to leave the hospital four days after the second application. No change had taken place in the local reaction up to that time.

Hypersensitivity Near the Area of Application: In none of these cases was this shown to be present before general hypersensitivity developed.

General Hypersensitivity: All three of the patients were tested for general hypersensitivity immediately before the second application and gave negative reactions then. The patient in case 9 who could be observed for only four days following the second application, did not show any flaring up of old skin reactions, and was not retested during that period. The other patients (cases 8 and 10) became generally hypersensitive. This was demonstrated in case 10 the twelfth day after the first application and the fifth day after the second. This was the first time that the patient was retested after the second application, and the local reaction was then at its height. In case 8 general hypersensitivity was discovered on the sixteenth day after the first application, the eighth day after the second, when the local inflammation had almost disappeared. The patient had not been retested between the second application and this time, as there had been no marked increase in the local reaction and no flaring up of old reactions.

Experiment 4.[11]—A patient (case 11), in whom the diagnosis was uncomplicated gonorrhea and who was negative to an eczema skin test with 10 per cent mesotan vaseline, was rubbed with sandpaper in an area 5 cm. in diameter above the left elbow crease, care being taken to prevent bleeding. Then 100 per cent

9. Bloch and Steiner-Wourlisch: Arch. f. Dermat. u. Syph. **152**:283, 1926.

10. The method of scraping the skin before the application to aid sensitization was first used by E. Cranston Low (Anaphylaxis and Sensitization, Edinburgh, W. Green and Son, Ltd., 1924, p. 175). Nägeli later used sandpaper, whereas Low had used a scalpel.

11. After the experiments had been terminated, Dr. Cohn, who was in charge of the ward in which the cases were under observation continued to retest some of the patients. She noted that the patient in case 11, who had not become hypersensitive in the sixteen days in which she was under observation, later showed a strong hypersensitive reaction, which was still present when she was again seen by me three months after the application.

mesotan was rubbed in for one minute and the area was covered with a piece of lint 5 cm. in diameter, soaked in 100 per cent mesotan, and with oiled silk and a bandage. The bandage was removed after twenty-four hours.

Local Reaction: The immediate local reaction was identical with that developed on the second application in the three cases in experiment 3. After a slight increase in the inflammation, the process gradually subsided.

Hypersensitivity Near the Area of Application and General Hypersensitivity: Up to sixteen days after the application, the patient had not developed hypersensitivity near the area of application or general hypersensitivity. These had been tested for four times in this period including the last day.

Addenda: Two further sets of observations were made which were not described in the foregoing sections. First, a number of the cases showed a flaring up of old skin reactions when new tests were applied, or on continued application of the drug in the local area. Secondly, the area of application was tested for hypersensitivity after the original local reaction had completely subsided. In this

TABLE 3.—*Results of Test for Hypersensitivity in Area Originally Treated*

Case	Number of Days after Last Application of Drug	Treated Area	Control
3	19	Vesicles, redness, infiltration and erythema surrounding whole originally treated area	Usual ++ reaction (redness and infiltration)
6	8	2.5 cm. vesicle on indurated and erythematous area	++
7	9	24 hours: faint erythema 48 hours: scattered papules where lint lay	24 hours: one papule with slight infiltration Erythema, slight infiltration where lint lay
8	13	Erythematous area covered with many tiny papules	++
10	12	++	++

series of tests, a corresponding area on the opposite arm was used as a control. The results were as shown in table 3.

It will be seen that in three cases the hypersensitivity in the healed local area was stronger than in the control region. In case 10 the reaction was approximately equal in the two areas and in case 7, which has already been shown to be peculiar in the time and type of reaction, the reaction in the treated area came on more slowly but was then more marked than on the control site.[12]

Summary: An attempt was made to sensitize eleven patients to mesotan: four with repeated consecutive inunctions with 10 per cent mesotan vaseline (experiment 1); three with repeated consecutive rubbings with 100 per cent mesotan (experiment 2); three with 100 per cent mesotan, first rubbing once without mechanical irritation and then, after an interval of seven or eight days, rubbing with sandpaper followed by an application of 100 per cent mesotan (experiment 3), and one with a single application of 100 per cent mesotan following a

12. Dr. Cohn later noted that the degree of local as well as general hypersensitivity varied from time to time and in some cases was cyclic.

rubbing with sandpaper (experiment 4). Five [13] of the eleven patients became generally hypersensitive.

In the first experiment one of the four patients became generally hypersensitive on the twenty-fifth day, and one became hypersensitive in an area near the site of applications on the thirty-fourth day. The patients who did not become generally hypersensitive were observed for thirty-five, thirty-two and twenty-nine days, respectively. In experiment 2, two of the three patients became generally hypersensitive on the eleventh day. The third patient had not become hypersensitive in eight days; after that time she could not be followed. In the third experiment, two of the three patients became generally hypersensitive on the twelfth and fifteenth day after the first application, the fifth and eighth day after the second application, respectively. The third patient had not become hypersensitive in eleven days after the first, four days after the second, application, when she was obliged to leave the hospital. The patient in the last experiment, the only one with a single application, did not become hypersensitive in sixteen days.

In addition to these patients, two (cases 1 and 2) became hypersensitive during the preliminary experiments after repeated applications of eczema skin tests (5 to 60 per cent mesotan) in varying areas; the first tests were applied from six to eight weeks, the last one from six to twelve days, before hypersensitivity was developed.

Besides these results, the following phenomena were noticed: (1) the flaring up of old eczema skin reactions; (2) a sudden increase in the severity and extent of local reactions; (3) a marked difference in one case (3) in the strength of hypersensitivity near the area of application and at a distance from it when the reactions first became positive, the adjacent area reacting more strongly at first but with equal strength later; (4) the development of hypersensitivity near the area of application, without the development of general hypersensitivity at the time (case 1), and (5) a stronger reaction in the healed area of local application than on a corresponding site on the other arm.

Experiment 5.—All the patients (cases A, B, 3, 6, 7, 8 and 10) who became generally hypersensitive were then tested to see whether their hypersensitivity was monovalent or polyvalent. The following eczema skin tests were applied on the back or chest.

The only substance other than mesotan to which any of the patients has been shown to be hypersensitive is a diluted solution of formaldehyde U. S. P. (1:10), and that reaction was elicited in only one case (9). This patient showed a doubtful reaction to formaldehyde when admitted to the hospital. It will be remembered in this connection, that in the presence of water a certain percentage of mesotan

13. Taking into account the observations later made by Dr. Cohn, the number of sensitized cases is raised from five to six of eleven treated patients (footnote 11).

splits into formaldehyde and salicylic acid. It is noteworthy that none of the patients was sensitized to salicylic acid.

Experiment 6.—All the patients (cases A, B, 3, 6, 7, 8 and 10) who became hypersensitive were tested with a scratch test to determine whether an urticarial element was present. Ten per cent mesotan vaseline was put on the skin, a cruciform scratch was made through the mesotan, and the area was gently rubbed for five seconds. Vaseline was used as a control. None of the patients developed a wheal in this test, although a mild 2 cm. erythematous zone was sometimes present for about fifteen minutes (this erythematous zone is also seen in some patients who have never been treated with mesotan, and give a negative reaction to a mesotan eczema skin test). It was concluded, therefore, that no urticarial element was present.

Experiment 7.—The serum of all seven patients (cases A, B, 3, 6, 7, 8 and 10) who became hypersensitive was tested for Prausnitz-Küstner[14] antibodies. The reactions, both immediate and late, were all negative except that in case A on one test person an urticarial wheal, 2 cm. in diameter, developed immediately after mesotan was applied percutaneously to one of the two areas in which serum

TABLE 4.—*Eczema Skin Tests for Polyvalency**

Substance Used in Test	A	B	3	6	7	8	10
Mesotan, 10% in oil	++	++	++	++	++	++	++
Mesotan, 5% in vaseline	..	..	++	++	++	++	++
Mesotan, 1% in oil	..	..	0	++	0	0	0
Vaseline	0	0	0	0	0	0	0
Salicylic acid, 10% in vaseline	0	0	0	0	+	0	+
Ethyl-acet-acetic acid, 10% in oil	0	0	0	0	0	0	0
Ethyl-methyl-acetic acid, 10% in oil	0	0	0	0	0	0	0
Ether, 10% in oil	0	0	0	0	0	0	0
Methyl salicylate, 10% in oil	0	0	0	0	0	0	0
Ammoniated mercury, 30% in vaseline	+	0	0	0	0	0	0
Formaldehyde, 10%	..	..	0	0	0	++	0
Odol	..	..	0	0	0	0	..
Potassium bromide or iodide, 25% in vaseline	..	..	0	0	0	0	0

* The symbol ++ means erythema with infiltration or hypersensitivity; + indicates mild erythema without infiltration and has been grouped with the 0 reactions.

from the patient in case A had been injected twenty-four hours previously. No such wheal appeared at the points of injection of control serums. This reaction could not be repeated on the same or other test persons and I do not know how to interpret it.

In cases 3, 8 and 10, an unsuccessful attempt was made to effect the passive transfer of hypersensitivity from serum taken from a bleb raised on the leg of each of these patients with carbon dioxide snow.[15] One tenth of a cubic centimeter of this serum was injected intracutaneously in the back of a test person; for a control, serum was used from a similar bleb raised on a nonhypersensitive subject. After

14. Prausnitz and Küstner: Zentralbl. f. Bakt. **86**:160, 1921.

15. This method was chosen according to the suggestion of Biberstein for the method of Königstein-Urbach-Perutz (Urbach, E.: Arch. f. Dermat. u. Syph. **154**:550 [Feb.] 1928) as a substitute for passively transferring antibodies supposedly present in the skin from blebs of the original lesion produced by an antigen or from blebs raised on a locally sensitized area. In the methods of Königstein-Urbach-Perutz there are certain doubtful factors (Biberstein, H.: Arch. f. Dermat. u. Syph. **154**:555 [Dec.] 1928) which are eliminated when the blebs are raised on previously untreated areas in which, nevertheless, a greater antibody content than that in the bloodstream might be assumed to be present.

twenty-four hours 10 per cent mesotan vaseline was applied percutaneously to the test person at the areas of injection. An immediate reaction was looked for; then an eczema skin test with 10 per cent mesotan vaseline was applied at the site of injection and was interpreted after twenty-four hours. The reactions were all negative.

Experiment 8.—An unsuccessful attempt was made to sensitize the skin of guinea-pigs and rabbits. Three methods of sensitization were used:

1. (Four rabbits.) A single rubbing with pure mesotan for one minute on an area of skin about 5 cm. in diameter (a single percutaneous application).

2. (Four guinea-pigs and three rabbits.) Repeated rubbings of the same area with 100 per cent mesotan on seven consecutive days (repeated percutaneous applications).

3. (Four rabbits and four guinea-pigs.) Single intracutaneous injections of 0.1 cc. of 20 per cent mesotan in olive oil (a single intracutaneous application).

No hypersensitivity could be disclosed by percutaneous or intracutaneous tests applied at intervals varying from ten days to five weeks.

COMMENT

As already stated there have been only a limited number of experiments similar to those described in this paper, dealing with the successful sensitization of the skin with substances of known chemical constitution by external application. Sauerland,[16] whose sensitization was an accidental result in an experiment on the absorption of drugs, worked with iothion and salicylate preparations, Lehner and Rajka[17] with allyl senföl (mustard oil) and cignolin-benzol, Biberstein[18] with sodium nirvanol, Frei[19] with neoarsphenamine, Schwarzschild[20] with the orthoform series and Nathan and Munk[21] with a brand of arsphenamine.[22] I will not describe in detail the research work with animals along these lines, as my results with animals were all negative (possibly due to the technical details of the methods employed), but will only

16. Sauerland, F.: Berl. klin. Wchnschr. **1**:629 (April) 1912.

17. Lehner and Rajka: Deutsche med. Wchnschr. **51**:825 (May) 1925; Krankheitsforsch. **5**:57, 1927.

18. Biberstein, H.: Med. Klin. **24**:557 (April) 1928.

19. Frei, W.: Klin. Wchnschr. **7**:539 (May) 1928.

20. Schwarzschild, L.: Arch. f. Dermat. u. Syph. **156**:432 (Aug.) 1928.

21. Nathan and Munk: Klin. Wchnschr. **7**:1125, 1928.

22. In addition to these experiments in which no protein was used in the sensitizing substance, Biberstein (Ztschr. f. Immunitätsforsch. u. exper. Therap. **48**:297, 1926) succeeded in sensitizing the skin of one person locally to mercury by repeatedly injecting intracutaneously, in various places, 0.1 cc. of serum containing 0.01 per cent of mercury bichloride. Three other patients similarly treated did not develop hypersensitivity, nor was Biberstein able to accomplish the same result with mercury bichloride in a watery solution. The one patient who was sensitized was hypersensitive not only to the mercury serum injected intracutaneously, but also to mercury ointments applied percutaneously to areas in which previous injections had been made.

mention that Walthard sensitized the skin of guinea-pigs to nickel sulphate,[23] Frei [24] and later Sulzberger [25] succeeded with neoarsphenamine and Mayer [8] with ursol.

Saureland,[16] who worked on himself, applied iothion, methyl salicylate, spirosal and saligenin percutaneously with successive applications on three sites. He became generally hypersensitive to all of these substances except methyl salicylate, and also found that he was now hypersensitive to 25 per cent mesotan. The method of procedure was too different from mine to allow of a detailed comparison, but this strikingly original experiment showed that experimental sensitization to chemical substances of known composition is possible.

Among Lehner and Rajka's [26] patients sensitized with allyl senföl (mustard oil), only one of nine persons treated became hypersensitive. The mode of application was similar to that in experiment 2. The time required before hypersensitivity appeared was approximately the same as in the cases in experiment 2, twelve days as compared with my result of eleven. In their case, however, Lehner and Rajka noted that there was an inborn, latent predisposition to sensitization, as the patient at the first application reacted more strongly to the allyl senföl (mustard oil) than the eight similarly treated patients who did not become hypersensitive. Such a predisposition could not be seen in the present cases, on the first application. The interesting experiment which these workers report of having caused anaphylactic shock in two guinea-pigs by preparing them one day with allyl senföl (mustard oil) rubbed into the ear and inhaled, followed the next day by the intraperitoneal injection of the sensitized patient's serum was not tried by me, but should certainly be attempted in the future.

In Lehner and Rajka's case of sensitization with cignolin benzol,[27] the method of application was again percutaneous; a 0.25 per cent solution of the substance was painted on daily. In one person out of ten, an inflammatory reaction set in locally on the eighth day, and his skin had then become generally hypersensitive. In this case Lehner and Rajka pointed out that the patient belonged to a hypersensitive family, as two other members of the same family (siblings) developed an arsphenamine dermatitis while being treated with that drug. No special histories were taken on this point in my cases. However, the relatively high proportion of positive results (five sensitized patients out of eleven in experiments 1 to 4) would suggest the unlikelihood of all of the sensitized patients belonging to so-called hypersensitive families.

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23. Walthard, B.: Schweiz med. Wchnschr. **7**:603 (June) 1926.
24. Frei, W.: Klin. Wchnschr. **7**:1026 (May) 1928.
25. Sulzberger, Marion B.: Klin. Wchnschr. **8**:253, 1929.
26. Lehner and Rajka (footnote 17, first reference).
27. Lehner and Rajka (footnote 17, second reference).

The work of Bloch and Steiner-Wourlisch [9] on primula is of utmost importance in this respect. The point deserves further careful investigation.

Biberstein [18] injected 0.0045 Gm. of sodium nirvanol intracutaneously into six persons; the injection was repeated on consecutive days. Four patients became generally hypersensitive, three who had received injections for eight days showed the reaction on the tenth day, one who had received injections for seven days showed it on the eighth day. His mode of application can best be compared to that of mine in experiment 2, in which two of three patients became generally hypersensitive in eleven days.

In Frei's [19] experiment with neoarsphenamine, the intracutaneous route was used. Of the sixty-six patients to whom one injection or repeated injections at widely spaced intervals (more than twelve days) were given, eight became hypersensitive, five after the first injection in from eleven to twelve days, and three in from seven to eight days after the second injection. The only case in my experiment which can compare to the first group is that in experiment 4 in which only one application was made after rubbing with sandpaper; this patient, who was observed for sixteen days, did not become hypersensitive in that time.[11] In repeated applications at a certain interval (experiment 3) two of three patients became generally hypersensitive the fifth and the eighth day after the second application. When Frei used daily intracutaneous injections for nine days, five of twelve patients became hypersensitive in from seven to nine days. This corresponds to experiment 2, in which two of three patients became hypersensitive in eleven days. Frei also observed the flaring-up phenomenon which I noted.

Nathan and Munk,[21] working with a brand of arsphenamine, also used the intracutaneous route. Of seventy-two patients who received one injection, nine became hypersensitive in from four to ten days. The flaring-up phenomenon was also noticed. The immediate general urticarial reaction which these workers noted in two cases has no analogy in the present series.

The experiment that most closely corresponds to the one described here is that of Schwarzschild [20] with the orthoform series; the mode of application for sensitization corresponds to that in experiemnt 1. He daily laid 10 per cent orthoform vaseline on the same area, bandaging after each application. Of 35 patients, eight became generally hypersensitive. One of the four cases in experiment 1 of my series showed this reaction. Schwarzschild's time of sensitization varied from ten to seventy-one days; in my cases sensitization resulted on the twenty-fifth day. In three of his cases after the local irritation had subsided he could demonstrate a period of temporary anergy. This was not seen in any of the present cases, irrespective of the mode of sensitization.[12]

Moreover, Schwarzschild did not find that the originally treated healed area reacted more strongly than the rest of the skin, while this phenomenon was clearly evident in some of my cases, including the patient sensitized with 10 per cent mesotan vaseline. These differences may of course depend on a different time interval of retesting. Schwarzchild also noted the flaring-up phenomenon. He tried, unsuccessfully, as I did, to transmit the hypersensitivity by the Prausnitz-Küstner test and to sensitize guinea-pigs and white mice. Finally, his sensitization, though not as strikingly monovalent as mine, was polyvalent within definite chemical groups.

There are, of course, many other important problems with which this study could profitably be compared. For the sake of brevity, however, I limited the description to those experiments in which sensitization of the skin of human beings has been voluntarily achieved with substances of known chemical composition by percutaneous or intracutaneous application.

CONCLUSIONS

Experiments 1 to 4.—1. It is possible to make a certain number of persons generally hypersensitive to mesotan (a substance of known chemical composition) by the application of the drug on a relatively small area of the skin (hypersensitivity of the type described by Jadassohn [28] as Ueber empfindlichkeit von aussen gegen von aussen.)

2. No definite conclusions can be drawn as to an incubation time. However, it seems indicated that an incubation period exists and that with a higher concentration of the drug applied, hypersensitivity develops more rapidly than with a lower.

3. It is possible for certain persons to become hypersensitive on the application of minimal quantities of mesotan (preliminary experiments).

Experiments 5, 6 and 7.—1. The type of hypersensitivity was monovalent with the exception of one patient (case 9) who reacted also to a diluted solution of formaldehyde U. S. P. (1:10). It is not known whether this was a true polyvalent reaction, or whether some of the mesotan in this case was decomposed into free salicylic acid and formaldehyde after application.

2. No urticarial element could be demonstrated in any of the cases by the scratch test.

3. No Prausnitz-Küstner antibodies could be demonstrated in the serum of hypersensitive patients or in blebs raised with carbon dioxide snow at a distance from the area of application. The observations that no urticarial element was present and that it was impossible to accom-

28. Jadassohn, J.: Klin. Wchnschr. **2**:1680 and 1734 (Sept.) 1923.

plish a passive transference of hypersensitivity would tend to support the theory that those hypersensitivities which call forth an eczematous [5] reaction cannot be passively transferred by the methods now available (Werner Jadassohn [29]). On the other hand, some workers (Perutz,[30] Fuhs and Riehl, Jr.[31]) report the passive transference of excematous hypersensitivity.

The following points deserve especial emphasis:

1. Every substance must, so far as sensitization is concerned, be observed and studied individually, and arguments by analogy can only be regarded as points for future investigation, not as conclusions.

2. The same substances excite very different reactions in different persons, so far as sensitization is concerned.

3. Local and general sensitizations do not appear regularly together; certainly, the former can sometimes be present without the latter.[28]

While bearing these points in mind, I hope that a further study of such experimental matters may help to throw light on the important field of skin diseases now classed as dermatitis or as eczema. I feel that the method used here for studying the problem is excellent for further experimentation: (1) because of the relatively high proportion of sensitizations obtained; (2) because the lesion produced in strongly sensitized areas belongs to the inflammations of the skin which involve the epidermis and cutis; (3) because the method when carefully applied (and I must caution against careless experimentation in this field especially when mechanical irritation is followed by the application of pure mesotan) is safe and simple with only a moderate degree of discomfort for the person being sensitized, and (4) because the sensitization seems to be strikingly monovalent toward a substance that is practically never to be met with in the normal environment.[32]

Wöllstrasse 19.

29. Jadassohn, Werner: Klin. Wchnschr. **5**:1957 (Oct.) 1926.

30. Perutz, A.: Arch. f. Dermat. u. Syph. **152**:617 (Dec.) 1926.

31. Fuhs and Riehl, Jr.: Arch. f. Dermat. u. Syph. **154**:88, 1928. Riehl, Jr.: Ibid. **157**:57 (Jan.) 1929.

32. I wish to acknowledge my indebtedness to Dr. H. Biberstein who performed the Praussnitz-Küstner and bleb tests with me.

MOLLUSCUM CONTAGIOSUM OF THE SCALP*

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As is well known, molluscum contagiosum can occur on any part of the body including the mucous membranes. The areas of predilection that are usually quoted are the face, breasts, genitalia and inner surfaces of the thighs. An opportunity was recently afforded me to see and treat a patient with such an infection confined exclusively to the scalp. Several internationally known dermatologists of many years' experience have informed me that they have never seen a case of molluscum contagiosum that involved the scalp alone. This was taken as sufficient reason to record, briefly, the chief clinical observations in the case reported.

REPORT OF CASE

A man, aged 34, a broker (a patient referred to Dr. A. W. Stillians) was first seen in July, 1929, at which time he complained of an eruption of the scalp of several months' duration, which was accompanied by a mild pruritus. The most annoying feature was the production of crusts when combing the hair. Examination of the scalp showed about thirty-five reddish follicular papules ranging in size from that of a pinhead to that of a split pea; the majority were situated on the parietal surfaces, and all were easily discernible because of marked alopecia of the scalp of the premature alopecia distribution type. The integument showed no involvement elsewhere, although the patient had had psoriasis at one time. The follicular type of lesions with localization to the scalp suggested the diagnosis of seborrheic dermatitis of the papular variety. The globoid contour with an occasional lesion presenting a minute whitish center brought up the possibility of molluscum contagiosum with an unusual distribution. Incision of several lesions with expression of molluscum bodies confirmed the diagnosis of molluscum contagiosum.

The usual method of treatment of incising each lesion and expressing the contents, followed by the application of iodine, was efficient. However, it was necessary to treat him several times, as new lesions appeared. It was impossible to determine the source of infection; the patient thought that he might have contracted it in a barber shop.

Crowley [1] was able to trace the infection in three cases to Turkish baths. These patients had the infection on their chests and abdomens.

Several instances were recorded in the recent literature of unusual and extremely localized areas of distribution of molluscum contagiosum.

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* Submitted for publication, Nov. 14, 1929.

1. Crowley, C. G.: Molluscum Contagiosum and Turkish Baths, Brit. J. Dermat. **41**:487 (May) 1929.

Young [2] reported the occurrence of such an eruption in a 2 months old girl, which started on the forehead and extended to the scalp. Kiefer [3] observed two cases in which the lesions were confined to the ocular regions; in one the lesions were confined to the lower lids, and in the other to the conjunctiva. Whitfield [4] recently described a miliary type of molluscum contagiosum. I recently observed a case in which there was only one lesion, which was situated on the left side of the neck.

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2. Young, W. J.: Molluscum Contagiosum with Unusual Distribution, Kentucky M. J. **24**:467 (Sept.) 1926.

3. Kiefer, H. A.: Molluscum Contagiosum, California & West. Med. **28**:490 (April) 1928.

4. Whitfield, Arthur: Molluscum Contagiosum Miliare, Brit. J. Dermat. **41**:10 (Jan.) 1929.

ETHYL IODIDE INHALATIONS IN THE TREATMENT OF MYCOTIC INFECTIONS OF THE SKIN AND ALLIED CONDITIONS*

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Iodides have been used for years in the treatment for blastomycosis, sporotrichosis and the like. The usual method of administration has been oral. More recently, the intravenous route has been resorted to. In view of the comparatively great loss of the drug when given orally and the rather varied results reported when given intravenously, we attempted to find a more direct means of getting the iodides to the affected areas. In addition, the fact that it is the belief of some, ourselves included,[1] that a number of mycotic infections are not simply local but hematogenous, caused us to seek a means whereby iodides could be introduced directly into the arterial blood. A simple way of doing this is to cause the patient to inhale some volatile iodide, such as ethyl iodide.

Ethyl iodide was chosen because of certain advantages which it offered. Ethyl iodide has been used extensively for the measurement of the minute volume output of the heart of man and has been found to be nontoxic and highly volatile. The coefficient of distribution between the alveolar air and the blood in the lungs is sufficiently high to allow introduction of a relatively large amount of iodine into the blood stream.

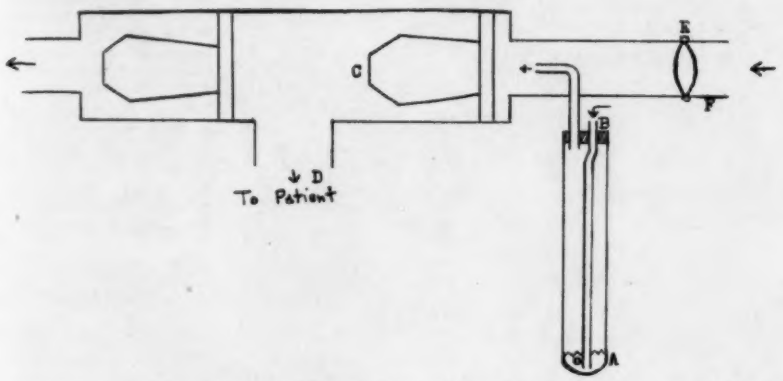
* Submitted for publication, Aug. 23, 1929.

* The work for this article was done with the aid of the DeLemar Mobile Research Fund.

1. Fried, S. M., and Segal, M. B.: The Hematogenous Production of Dermatomycoses, Arch. Dermat. & Syph. **19**:98 (Jan.) 1929. Kogoj, F.: Experimentelle Beiträge zur Lehre von den Dermatomykosen, Arch. f. Dermat. u. Syph. **150**:331, 1926. Ambrosoli, G. A.: Coltura di trychophyton Gypseum del Sangue Circolaute in Trichofizia Profonda con Lichen Trichophyticus, Gior. ital. d. mal. ven. **62**:233, 1921. Jessuer, M.: Zur Pathogenese der Trichophytide, Arch. f. Dermat. u. Syph. **136**:416, 1921. Passini, A.: Zur Trichophytonkultur aus den zierkulierluden Blute bei Trichophytiden, Arch. f. Dermat. u. Syph. **140**:369, 1921. Sutter, E.: Zur Kenntnis der Pathogenese der Trichophytide, Arch. f. Dermat. u. Syph. **127**:735, 1919.

It has been demonstrated, moreover, that only a small proportion is returned in the venous blood, so that the tissues are exposed to relatively large amounts of iodine.[2]

It was found that ethyl iodide vapor when not diluted with large quantities of air is unpleasant to the taste and often irritating to the mucous membranes. Accordingly, we devised an apparatus that enables us to administer any given quantity of the drug with no discomfort to the patient. Ethyl iodide at ordinary temperatures is a liquid, but is exceedingly volatile. A draft of air is sufficient to vaporize it. We therefore place the desired quantity of the liquid ethyl iodide in the tube marked *A* so that as the patient inhales, a stream of air is bubbled through it from tube *B*. The ethyl iodide-laden air is carried through the one-way valve *C* to the patient's mouth and so into the lungs. The



Apparatus for administering ethyl iodide without discomfort to the patient.

system of valves pictured is necessary to prevent backwash through the liquid. The rate at which the liquid evaporates can be controlled by varying the amount of air bubbling through it. This in turn can be regulated by partly opening or closing stopcock *E*. That is, the less air that goes through tube *F*, the more will have to go through *B*, and the amount of air going through tube *F* depends on how far stopcock *E* is open. The apparatus is fitted with a rubber mouthpiece, *D*, such as is ordinarily used on a respiration apparatus, and the patient's nose is pinched off with a clamp so that he is forced to breathe through the apparatus. He suffers no more discomfort than he would during the ordinary determination of the basal metabolic rate.

The dosage has not been carefully worked out as yet, but at present we are getting good results by permitting adult patients to inhale 2

2. Henderson, Y., and Haggard, H. W.: The Circulation and Its Measurement, Am. J. Physiol. **73**:193, 1925.

Results of Inhalations of Ethyl Iodide

Name	Diagnosis	Parts Involved	Duration	Number of Treatments	Remarks
S. G.	Epidermophytosis	Hands	2 years	9	Almost completely cleared
S. M.	Epidermophytosis	Hands, feet (extensive involvement)	3 months	13	Marked improvement
R. M.	Epidermophytosis	Groins and under breasts	14 months	10	Perfectly clear, but itched somewhat
A. S.	Epidermophytosis		3 months	16	Much improved after 10th treatment
R. T.	Epidermophytosis	Palms and interdigital spaces	1 year	13	Much improved after 6th treatment; continued slower improvement; almost entirely clear
L. P.	Epidermophytosis	Hands, feet	4 years	11	Perfectly clear; discharged
M. F.	Epidermophytosis	Hands, feet (extensive involvement)	2 to 3 years	6	Itching which was severe, gone; no activity; dry scaly skin left; improved
P. R.	Epidermophytosis	Hands, feet	2 years	6	Improved
A. S.	Epidermophytosis	Hands	23 years	7	Had tried all known forms of treatment without success; marked improvement after second treatment; continued improvement since
Dr. S.	Epidermophytosis	Feet	2 years	6	Improved after second treatment; slight relapse, now practically clear
L. B.	Epidermophytosis	Hands	4 years	6	Lesions clearing; itching gone
M. M.	Epidermophytosis	Feet	1 year	7	No itching; clinically practically clear
L. T.	Epidermophytosis	Groins and intergluteal fold (extensive involvement)	Many years	2	Had tried a variety of remedies; completely clear after two treatments
Mrs. C.	Epidermophytosis	Hands, feet (extensive involvement)	3 years	4	Itching which was marked, gone; clinically much better
C.	Epidermophytosis	Feet	2 years	4	Itching gone; clinically improved
M. M.	Epidermophytosis	Hands	2 years	1	No change
M. F.	Epidermophytosis	Intergluteal fold and groins (extensive involvement	15 years	4	Itching was severe, now gone; clinically improved; patient had been both a ward and an outpatient case at various hospitals, but had at no time been able to obtain sufficient relief
V. Z.	Favus	Scalp	2 years	10	Improvement began after second treatment; continued improvement; after tenth treatment patient showed absence of crusts, leaving clean looking atrophic areas
W. D.	Blastomycosis	Upper and lower extremities	1 year	16	Marked improvement after second treatment; slower improvement since
F.	Tinea capitis	Scalp	?	6	Not much change
P.	Tinea circinata	Neck, anterior, chest, arms	3 weeks	5	Clear; no activity
F. M.	Cryptococcosis epidermica		Since childhood	6	Decided improvement symptomatically and clinically
P. G.	Cryptococcosis epidermica		18 years	5	Symptomatically improved; clinical picture unchanged
S.	Cryptococcosis epidermica		2 weeks	4	Almost clear; itching gone
W.	Cryptococcosis epidermica		Years	2	No change

Results of Inhalations of Ethyl Iodide—Continued

Name	Diagnosis	Parts Involved	Duration	Number of Treatments	Remarks
A. F.	Psoriasis	Scalp, face, trunk and extremities	11 years	19	Reaction (headache and dizziness) after sixteenth treatment; lesions changed in appearance, i. e., less parakeratosis; itching fairly marked
F.	Psoriasis		Several months	18	Less itching after fourth treatment; clinical improvement after sixteenth treatment
R.	Juvenile psoriasis		1 year	8	Much improved after fourth treatment
P.	Psoriasis; arthritis	Generalized	Many years	4	Little change
F.	Psoriasis		?	8	No change
C. G.	Seborrheic eczema; pityriasis rosea	Scalp, face, arms, umbilical and pubic regions	5 months	6	Improved clinically and symptomatically
		Trunk	3 weeks		Completely cleared
S.	Seborrheic eczema		12 years	5	No change
B. K.	Pityriasis rosea		1 week	14	Completely cleared after twelfth treatment

Gm. (1 cc.), and children half of that. We spread the inhalation time of this quantity of the drug over about twenty minutes.

No local applications other than petrolatum have been permitted during the course of treatment.

Our results thus far are given in the accompanying table.

The clinical diagnosis of fungus infection has been verified by microscopic examination of scrapings and by cultural studies in practically every one of the listed cases.

SUMMARY

Iodides have been used in mycotic infections for many years. The methods of administration have been oral and intravenous. Inhalation has not been used previously. Ethyl iodide is nontoxic and is easily administered by the method described. Children may be treated as well as adults. It has thus far proved successful, particularly in epidermophytosis, which is known to show stubborn resistance to all sorts of treatment. Epidermophytosis involving the groins and intergluteal fold responds the quickest. A more detailed report will follow later.

Because of the results obtained, this method of treatment should be tried in other conditions in which iodides appear to be useful, particularly asthma, hypertension and tertiary syphilis.

NOTE.—Since this article was submitted for publication, we have found that daily treatments are more effective than treatments given on alternate days.

EXPERIMENTAL URTICARIA

ITS RELATION TO SPONTANEOUS URTICARIA*

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Among the skin diseases that are now usually considered under the term "allergic condition," urticaria plays a prominent part. In all these diseases the question of sensitization and desensitization occupies at present a place of primary importance. The problem is especially difficult to grasp clinically and experimentally. It has been found that urticaria of internal origin has a counterpart in that of external origin, namely, the artificial wheal. The clinical and, as far as is known, the histologic pictures of both conditions have so much in common that there is little reason to assume any important differences in their local genesis. On this general basis it is hoped, by the study of the artificial wheal, to arrive at some justifiable conclusions as to its relation to spontaneous urticaria.

One is inclined to regard some of the manifestations of so-called spontaneous urticaria as phenomena of sensitization and desensitization; in the first place, there are the well known alternation of periods of eruption and intervals of freedom. But it is hardly possible here to exclude the intermittent liberation of urticariogenic substances. Some cases, those of urticaria due to cold, for example, seem to suggest that as a result of external irritation with cold the urticariogenic substances pass into the circulation. An analogy might be assumed, for instance, in urticaria of intestinal origin.

In the second place, the localization of spontaneous urticaria might well be employed with the thought of sensitization as well as desensitization, as there are, on the one hand, cases in which the same areas are again and again affected and, on the other hand, instances in which new areas are involved each time. The course of spontaneous urticaria, however, is extraordinarily variable in its localization, and such conclusions must be guarded against.

In the third place, there is also the desensitizing therapy which has been successful in some cases.

All these facts do not suffice, however, to identify the intermittent course of endogenous urticaria with sensitization and desensitization, but they render it highly desirable to collect, if possible, extensive

* Submitted for publication, Aug. 14, 1929.

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experiences with this form, that is, the artificially produced ectogenous urticaria.

Observations on the course of experimental wheals repeatedly produced on the same areas of skin are reported in the literature, but the results generally do not agree, so that it is necessary to supplement this work. Moreover, there is the possibility that such observations may throw some light on the question of the pathogenesis of urticarial processes, which is not yet definitely explained.

When I speak of sensitization and desensitization I mean the increase or diminution of the reaction without any reference to the special relations of the question of allergy.

The following experiments have been made on human skin, as well as on that of dogs, and the results on the latter are reported and compared with those on the former. Although the experiments on dogs, which will be referred to later, did not show any significant differences, the advantage was that the eruption was produced freely. Dogs are especially useful for histologic researches.

A great many observations have been recorded in the literature concerning the local urticarial reaction of the skin to repeated mechanical or chemical irritation. Ferré and Lamy,[1] in 1892 (later, Ebbecke,[2] Lewis and Grant,[3] Duke [4] and Vallery-Radot and co-workers [5]), reported that in cases of urticaria factitia, repeated mechanical irritation on the same cutaneous areas produced a relative immunity, so that the skin after recovering from the first application reacted much more weakly or was immune to a second irritation. Weidenfeld,[6] in 1910, noted, however, no such hyposensitiveness.

Török and Hari [7] found that after repeated intradermal injections of atropine the skin was rendered hypersensitive, and that on injection of a nonurticariogenic substance even the surrounding area reacted with wheal formation. But Merklen,[8] in 1904, made the observation, later confirmed by Ebbecke but denied by Low,[9] that the development of a

1. Ferré and Lamy, cited by Barthelemy: II International dermatologische Kongress, Wien, 1892, p. 545.

2. Ebbecke, U.: Arch. f. d. ges. Physiol. **168**:1, 1917.

3. Lewis, T., and Grant, R. T.: Heart **2**:209, 1924.

4. Duke, W. W.: Allergy, Asthma, Hay Fever, London, Henry Kimpton, 1925, p. 26.

5. Vallery-Radot, Pasteur; Krief, Jacques; and Jacquemaire, Réné: Presse méd. **32**:517, 1924.

6. Weidenfeld, S.: Arch. f. Dermat. u. Syph. **99**:22, 1910.

7. Török, L., and Hari, P.: Arch. f. Dermat. u. Syph. **65**:21, 1903.

8. Merklen, P.: Pratique dermatologique, 1904, vol. 4, p. 738.

9. Low, C.: Anaphylaxis and Sensitisation, Edinburgh, W. Green and Son, 1924, p. 35.

wheal from nettle was suppressed when the same area of the skin was brought in contact with this substance three or four times.

A systematic study of the local tolerance of the skin was made, in 1914, by Jadassohn and Rothe,[10] who were able, by repeated injections of morphine in the same spots at certain intervals, to produce a kind of local tolerance. They found that after recovering from morphine the area was tolerant to atropine, but that after atropine it was not tolerant to morphine. In two cases of internal urticaria of unknown etiology, the involuting wheals were shown to react less violently to intradermal injections of morphine than the normal skin.

Sollman and Pilcher,[11] repeating the experiments of Jadassohn and Rothe, also observed that when repeated applications of histamine were made by the mucuna method the wheals resulting from the later applications appeared smaller than those of the earlier, but in another study made later they failed to note these differences. Hecht,[12] in an observation on skin allergy, reported that the same area of the skin reacted more feebly to the fourth injection of atropine than to the first; similarly von Gröer and Hecht[13] found that following a previous intradermal injection of morphine the same area was hyposensitive to a later injection of the same substance. More recently, Lewis and Grant reported that a similar area of skin after mechanical irritation was also tolerant to histamine administered by puncture. Likewise they noted that after the administration of histamine the area was tolerant not only to further administration of this drug but also to mechanical irritation. Ebbecke also reported that the wheal which developed after repeated injections of peptone was definitely smaller than that following a single injection.

Török, Lehner and Urban,[14] in a recent extensive investigation of the problem, reported that when chemical or mechanical irritations were repeated at intervals of fifteen minutes, one hour or twenty-four hours, the wheal and the surrounding erythema increased in size after the first two or three repetitions of the injections, but that a diminuition of the reactions to even less than normal was observed after further repetitions. This phenomenon was not specific, although the increase and decrease of the reactions were more marked when the same substance was used.

A perusal of the literature, shows that the question of local cutaneous reaction, especially to repeated chemical irritations, has not

10. Jadassohn, J., and Rothe, L.: Berl. klin. Wchnschr. **2**:519, 1914.

11. Sollman, T., and Pilcher, J. D.: J. Pharmacol. & Exper. Therap. **9**:309, 1917; **10**:147, 1917.

12. Hecht, A.: Wien. klin. Wchnschr. **47**:1023, 1920.

13. Von Gröer, and Hecht, A.: Ztschr. f. d. ges. exper. Med. **35**:Hi/2, 1923.

14. Török, L.; Lehner, E., and Urban, F.: Krankheitsforsch. **1**:371, 1925.

yet been answered. I have, in consequence, undertaken to make further experimental observations on the subject.

Before proceeding to describe the experiments, it is necessary to define what is meant by urticaria. Most textbooks include urticaria vesiculosa or bullosa under urticaria. These cases may be etiologically analogous, but they cannot be completely identified pathogenically. In my opinion, urticaria, as Jadassohn and Rothe emphasized, should be limited to the superficially located, sharply circumscribed and elevated edema of the skin with surrounding hyperemia. This condition is further characterized by its acute onset and rapid subsidence.

TECHNIC

I am indebted to Philippson[15] for a method by which a wheal can be easily produced on human subjects and animals, especially dogs. He produced clinically typical wheals by injecting a small quantity of the solution of morphine, atropine or peptone into the upper layer of the cutis by means of a fine capillary glass tube. These experiments were later confirmed by Török and Hari and by others. I employed in my study the same method as that used by Sollman and Pilcher, and later extensively by Lewis and his co-workers. A drop of the solution to be tested is placed on the skin and a puncture is made with a sharp needle vertically through it and the epidermis. Because of the small amount of the substance introduced, the wheal is naturally smaller than that produced with the intradermal injection, but the reaction is usually distinct and large enough to permit a detailed study of the various features of the wheal.

A description of a wheal thus produced will naturally be more or less diagrammatic, because minor variations will occur in the duration of the latent period, the time for the maximal development and the size and duration of the reaction. They are not marked, however, in these experiments, and from frequent repetitions useful results are obtained for comparative study.

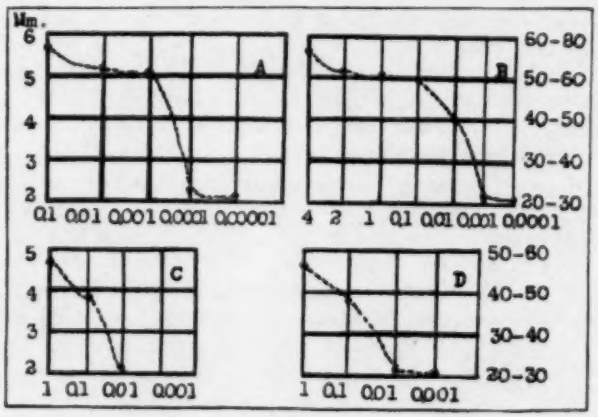
Thus, when a solution of urticariogenic substance (morphine 1:100) is introduced as described, in from twenty to thirty seconds there appears around the prick a diffuse erythema from about 15 to 25 mm. in diameter, the central part of which gradually becomes deeper in color; in from two to three minutes there develops in its place a sharply demarcated, distinctly palpable and elevated wheal, which reaches its maximum size of about 5 or 6 mm. in from five to seven minutes. As the wheal increases in size and prominence, it becomes paler; for fifteen or twenty minutes it remains stationary; then it loses its sharp contour and gradually subsides. The surrounding erythema begins to fade in from ten to twenty minutes after the puncture and disappears completely in about half an hour, but the wheal itself does not vanish until after from sixty to eighty minutes, and its position is recognizable for a considerable time by the pinhead erythema around the prick. All the wheals in the present experiments appeared almost without exception as described, and I failed to corroborate Winternitz' observation on his own arm, that one day he produced a distinct wheal and on another day a barely elevated efflorescence. I found, however, a difference in the size and prominence of the reaction, depending on whether it was produced on the flexor or on the extensor surface of the arm. Well developed wheals are easily produced on the flexor surface round the elbow. All my experimental study, therefore, was conducted on this region.

15. Philippson, L.: Gior. ital. d. mal. ven. e. d. pelle **34**:675, 1899.

EXPERIMENTAL WORK

EXPERIMENT 1: *The influence of Dilutions on Wheal Formation.*—As the interpretation of experiments requires an idea of the degree of reaction produced by different concentrations of the various urticariogenic substances so as to give results suitable for comparison, I determined the different concentrations of these substances that would produce wheals approximately similar in size and duration. The diluent used in this work was physiologic solution of sodium chloride. In order to avoid repetitions of description, the results are represented in the accompanying diagrams.

The diagrams show that the degree of the reaction of the urticariogenic substances in the higher concentrations varies little in proportion to the dilutions. For example, the wheals produced with 4 per cent morphine or 0.1 per cent histamine were almost identical with those of 0.1 per cent morphine or 0.001 per cent histamine. There were, however, individual differences for each drug. When the dilutions were further diminished, the reaction curves were again almost equal.



The reaction produced by dilutions of four urticariogenic substances: *A*, histamine; *B*, morphine; *C*, atropine, and *D*, pilocarpine. The size of the wheal is indicated in millimeters on the vertical scale at the left, the duration of the reaction in minutes at the right, and the dilution in per cent on the horizontal scales.

The wheals produced by the weaker dilutions with the puncture method were small and distinguishable from those of simple trauma only by their greater prominence and duration.

In order to make certain that the wheals described were due to chemical ingredients, the reactions to the diluent and the puncture were also determined and the following was noted:

After puncture with the needle there appeared a slight erythema around the prick. In from two to four minutes there developed a barely infiltrated elevation the size of a pinhead, which disappeared in from fifteen to twenty minutes. When a physiologic solution of sodium chloride was used, the reaction was almost the same as that caused by a simple puncture, except that the infiltration was more marked.

EXPERIMENT 2: *Skin Reactions to Repeated Injections, at Half Hour Intervals, of an Urticariogenic Substance of the Same Dilution.*—After determining

the reactions to the various agents used in this study, the next observation was made on the reaction of the skin when the same area received repeated injections, at half hour intervals, of solutions of morphine 1:1,000, histamine 1:10,000, atropine 1:100 or pilocarpine 1:100, respectively. The first repuncture was made on an involuting wheal, but subsequent repetition was made on an area in which no wheal was recognizable. In all, five or six punctures were made on each spot with the respective substances. It was observed that with the first repetition a diffuse erythema was produced of about the same proportion as that of the first puncture, while the previously subsiding wheal continued to regress. With the second and further repetitions, the erythematous reactions became smaller, and no definite wheal formation was noted at any of the sites of repeated punctures. Finally, a moderately deep, diffuse swelling was produced, which lasted for twenty-four hours.

EXPERIMENT 3: *Skin Reactions to Repeated Punctures at Half Hour Intervals with an Urticariogenic Substance of Progressively Increasing Concentrations.*—When the foregoing experiment was repeated by using for each puncture solutions of progressively higher concentrations (for example, with morphine the first solution used was 1:10,000, the second 1:1,000, and so on), results identical with those described were observed, with the exception that the erythema and diffuse infiltration with each subsequent puncture were more marked.

In the two foregoing experiments, there was definitely shown the exhaustion of the skin reaction following repeated introductions of solutions of the same or higher concentrations at certain intervals. These results are corroborative of the observations of Jadassohn and Rothe and others on chemical urticaria, and also those of Ferré and Lamy, Ebbecke and others on urticaria factitia. In none of the repeated punctures did I notice any increase in the size of the wheal or the erythema, as reported by Török, Lehner and Urban. It is possible that this difference in results might be accounted for by the varying methods of injection, as well as by the intervals between injections adopted by these authors.

EXPERIMENT 4: *Skin Reactions to Repeated Punctures with an Urticariogenic Substance of the Same Dilution at Progressively Longer Intervals.*—In view of the result of the foregoing experiment, the next step of the study was to determine the duration of this abolition of reaction. Instead of puncturing at half hour intervals, repetitions were therefore made after progressively longer periods. Accordingly, one hour after the first puncture a second was made on the same spot with the identical solution, and simultaneously a control introduction was made in the adjacent area. Whereas on the latter area a typical wheal developed, on the former there was only a diffuse erythema with slight infiltration in the center, which lasted from about twenty to thirty minutes. After two hours, the same area was again punctured, with a similar result. This operation was repeated after another three hours, and the process was continued in this fashion. In this way, the intervals which elapsed before wheals of normal size could be produced with the different substances were determined and are appended in table 1.

EXPERIMENT 5: *Skin Reactions to a Repeated Introduction by Puncture of an Urticariogenic Substance of the Same Dilution at Various Intervals.*—As the phenomenon of tolerance in the preceding experiment was brought about by a series of punctures, the technic was modified in such a way as to determine the duration of the desensitization by a single previous puncture. A number of wheals were produced at the same time. At the end of the first hour, a repetition of the puncture was made on the site of the first wheal with the same substance, at the end of the second hour on that of the second, at the end of the third hour on that of the third, and so on. In this way, only a second puncture was performed

on each area, and that at longer intervals was made on apparently normal skin. The results are appended in table 2.

It is seen in experiments 4 and 5 that the wheal caused by morphine exercised the greatest desensitizing effect, although the size and duration of the wheal were about the same as those produced by other substances in their respective concentrations. The differences between the other substances in this respect were insignificant. It is shown that the size of the wheal is not the determining factor in desensitization, but that another influence must play a part; this might be, for example, the difference "remnant" of the individual substance.

EXPERIMENT 6: *Skin Reactions to a Repeated Puncture with an Urticariogenic Substance of Progressively Increasing Concentrations at Various Intervals.*—While variable periods of tolerance were demonstrated in the foregoing observa-

TABLE 1.—*Intervals Between Repeated Injections of Urticariogenic Substances in Man and in Dogs and the Production of a Normal Wheal*

Substance	Dilution, per Cent	Subject	Interval, Hours
Morphine	1	Man	10-12
	0.1	Dog	5-7
Histamine	0.01	Man	5-7
	0.001	Dog	3-4
Atropine	1	Man	5-7
	1	Dog	5-7
Pilocarpine	1	Man	5-7
	1	Dog	3-4

TABLE 2.—*Interval Between the Injection of an Urticariogenic Substance, Once Repeated, in Man and Dogs and the Production of a Normal Wheal*

Substance	Dilution, per Cent	Subject	Interval, Hours
Morphine	1	Man	7-9
	0.1	Dog	5-6
Histamine	0.01	Man	4-6
	0.001	Dog	2-3
Atropine	1	Man	4-5
	1	Dog	3-4
Pilocarpine	1	Man	5-6
	1	Dog	3-4

tions, it would be interesting next to determine whether the duration of this phase of tolerance would be influenced when solutions of higher or lower concentrations were used for repeated punctures. For example, with morphine the dilution for first puncture was 1:1,000, and that for the subsequent puncture 1:100, and vice versa. Here also definite tolerance was observed, but the tolerance against the repuncture of higher concentration was somewhat shorter, and that with the lower concentration was longer than when the same dilution was used.

EXPERIMENT 7.—*The Desensitizing Effect of Morphine, Histamine, Atropine and Pilocarpine Against Each Other.*—The experiments thus far have clearly shown that when the same area of skin was subjected to repeated punctures of the same substances, a certain degree of local tolerance seemed to develop, the duration of which varied to a slight extent with the concentrations of the solutions used for the repetitions. As Jadassohn and Rothe have pointed out the difference in the desensitizing action of atropine and morphine, it would be of importance here to supplement their observations on a larger scale. The experiment was conducted

in the same way as experiment 6, except that solutions of substances different from those used in the first punctures were employed for the repetitions. The results are shown in table 3.

Table 3 shows that morphine produces the strongest desensitizing effect against all other substances, next histamine and then atropine and pilocarpine. It further shows that the desensitization against subsequent punctures with morphine is weaker than that against the other substances, and among these the desensitization against histamine is also weaker than that against atropine and pilocarpine. This means that morphine occupies a special place in its desensitizing influence, a feature which does not correspond to the intensity of the wheal which it causes; histamine comes next, and the effect of atropine and pilocarpine is about equal. The weaker urticariogenic substances cause less of a desensitizing effect against the stronger substances than the latter against the former.

TABLE 3.—*The Desensitizing Effect of Morphine, Histamine, Atropine and Pilocarpine Against Each Other*

Substance Used for First Puncture	Dilution, per Cent	Substance Used for Subsequent Puncture	Dilution, per Cent	Subject	Interval, Hours
Morphine	1	Histamine	0.01	Man	6-8
Morphine	0.1	Histamine	0.001	Dog	3-4
Morphine	0.1	Atropine	1	Man	10-12
Morphine	0.1	Atropine	1	Dog	3-4
Morphine	0.1	Pilocarpine	1	Man	8-9
Morphine	0.1	Pilocarpine	1	Dog	4-5
Histamine	0.01	Morphine	1	Man	4-6
Histamine	0.001	Morphine	0.1	Dog	2-3
Histamine	0.01	Atropine	1	Man	6-8
Histamine	0.001	Atropine	.	Dog	3-4
Histamine	0.01	Pilocarpine	1	Man	7-8
Histamine	0.001	Pilocarpine	.	Dog	3-4
Atropine	1	Morphine	0.1	Man	2-3
Atropine	1	Morphine	.	Dog	1-2
Atropine	1	Histamine	0.01	Man	3-4
Atropine	1	Histamine	0.001	Dog	1-2
Atropine	1	Pilocarpine	1	Man	5-7
Atropine	1	Pilocarpine	1	Dog	2-3
Pilocarpine	1	Morphine	0.1	Man	2-3
Pilocarpine	1	Morphine	0.1	Dog	1-2
Pilocarpine	1	Histamine	0.01	Man	2-3
Pilocarpine	1	Histamine	0.001	Dog	1-2
Pilocarpine	1	Atropine	1	Man	5-6
Pilocarpine	1	Atropine	1	Dog	2-3

Thus it is possible, at present, to say: Both the stronger urticaria-producing substances have the greatest desensitizing effect against other substances, and the desensitization against them is of the shortest duration, i.e., the weakest. But here again, morphine possesses a special property.

EXPERIMENT 8: *The Influence of Epinephrine on Wheals (Chemical) Locally and of Wheal Formation on Epinephrine Anemia.*—Further experiments were undertaken specially with a view to determining whether the desensitization after the production of wheals by a chemical substance would be influenced by epinephrine or not. For this purpose it was necessary, first of all, to determine the effect of epinephrine on wheals of this kind. Although the influence of epinephrine on urticarial eruption has long been known, little work has been done on its

action on a wheal locally. Baum, and later Vallery-Radot and his co-workers, reported that the injection of epinephrine in urticaria factitia produced a flattening of the wheal; Weidenfeld, on the contrary, found that it had no influence on the edema, except that it rendered it anemic. Jadassohn and Rothe repeated the study and reported that on the injection of epinephrine into a fully developed morphine wheal, they noted a quickening of the involution of the wheal. This observation was later confirmed by Sollman and Pilcher.

Baum, Weidenfeld and others found that it was not possible to produce a wheal with mechanical irritation, and Sollman and Pilcher that it was not possible with the application of morphine or histamine to an area rendered anemic by epinephrine. Török and Rajka and Lewis and Grant reported that typical wheals could be produced with an urticariogenic substance on an anemic area of this kind.

In view of the contradictory results reported by different workers and the possible significant bearing of such an observation on the pathogenesis of urticaria, I was obliged to repeat some of the experiments on the relation of epinephrine to chemical wheals, and the action of urticariogenic substances on epinephrine anemia. I was able to confirm the observations of Jadassohn and Rothe on the effect of epinephrine on chemical wheals, and those of Török and Rajka, and Lewis and Grant on the action of urticariogenic substances on epinephrine anemia; in addition, I noted that a wheal produced on an anemic area disappeared more rapidly than that produced on the normal skin.

EXPERIMENT 9: *The Skin Reaction from a Mixture of Epinephrine and an Urticariogenic Substance.*—To determine whether or not epinephrine has any influence on the desensitization, the simplest method was to mix it with the urticariogenic substance and to study the reaction of this mixture. Should the wheal fail to develop, the observation on the desensitization could be studied further. By using a mixture of varying concentrations of epinephrine with a constant dilution of urticariogenic substance, I observed a wheal in accordance with the concentration of the epinephrine. When epinephrine 1:1,000,000, mixed with an equal part of morphine 1:1,000, histamine 1:100,000, atropine 1:100 or pilocarpine 1:100, brought into the skin by puncture, it gave rise to a diffuse erythema which was also present with puncture of epinephrine alone and hardly distinguishable from simple trauma; the erythema lasted from ten to fifteen minutes, but no definite wheal or anemia was produced. When, however, a stronger dilution of epinephrine or an urticariogenic substance was used, anemia or a wheal developed accordingly.

The influence of epinephrine on wheals is interesting in that it not only hastens the regression of the wheal, but also hinders its formation when introduced by puncture in a mixture with an urticariogenic substance. To explain this fact, it must be assumed either that epinephrine enters into a chemical reaction with the urticariogen or that it counteracts its action when introduced by puncture.

EXPERIMENT 10: *Desensitization When Wheal Formation Was Suppressed by Epinephrine.*—After having determined the reaction to a mixture of epinephrine and an urticariogenic substance, an experiment was performed to determine whether or not an area that had previously been treated with this mixture, in which wheal formation was suppressed, would develop tolerance to a subsequent introduction by puncture of the urticariogenic substance in the mixture. By repeating the punctures with the urticariogenic substance at intervals of one-half hour, one hour, and so on, on different areas that had previously been treated with the mixture, it was possible to produce smaller wheals after a lapse of from one to two hours, but at the end of two hours those comparable to the control wheals on normal skin developed. Although transient tolerance was definitely

shown, it seemed that the previous wheal formation played an important part in determining the duration of this phase.

EXPERIMENT 11: *Wheal Formation from an Urticariogenic Substance Introduced into the Skin After the Disappearance of Epinephrine Anemia.*—It is not known whether epinephrine possesses an urticariogenic potency or not; it is possibly hidden by the anemic effect of the drug. If such a property is present, then the wheal can only be latent and clinically unrecognizable. The determination of whether a latent wheal exists after the introduction of epinephrine seems to be of great importance.

As it was shown that the refractory phase was associated, to a great extent, with the previous wheal formation, I demonstrated this after epinephrine was introduced by puncture. Anemia was produced with epinephrine 1:10,000, and after its disappearance (usually at the end of an hour), morphine 1:1,000 was introduced in the same spot. The wheal thus produced was found to be the same as that on the normal skin. This experiment shows that if there had been a latent wheal after the introduction of epinephrine by puncture, a change in the wheal formation would have been expected from morphine subsequently introduced.

Analogous observations were made on dogs. In agreement with Török and Hari, I found that the region on the abdomen near the genitalia was most suitable for the production of wheals. Among the dogs at my disposal, I observed little variation in wheal reaction, except that on the younger dogs less marked wheals seemed to develop. An increased sensitiveness after repeated injections, as reported by Török and Hari, was not observed. The results corresponded closely to those observed in human subjects.

SUMMARY AND COMMENT

1. In the foregoing experiments a local desensitizing effect following wheals produced by chemical substances, such as morphine, histamine, atropine or pilocarpine, has been regularly observed. The negative results of other authors might be accounted for by the difference in the intervals at which repetitions were made or in the method employed. Morphine seemed to give the highest desensitizing effect, although in the concentrations used, the wheals were similar in almost all respects to those produced with other substances. Conversely, the desensitization accounted for by other substances was of the shortest duration against morphine.

2. Epinephrine introduced by puncture into a fully developed chemical wheal produced anemia and hastened the involution of the wheal. Wheals could be produced with the different urticariogenic substances on areas rendered anemic by epinephrine, and were observed to undergo involution earlier than those on the normal skin. When a mixture of epinephrine and an urticariogenic substance was introduced into the skin, a wheal or anemia developed according to the concentration of epinephrine in the mixture. Epinephrine 1:100,000 in equal parts with morphine 1:1,000, histamine 1:100,000, atropine 1:100 or pilocarpine 1:100 gives rise to no definite wheal formation or anemia. With a higher concentration of epinephrine, anemia is produced. An area of skin previously treated with such a mixture, in which wheal

formation was suppressed, also showed refractoriness to a subsequent injection of the urticariogenic substance.

3. The numerous theories on the genesis of urticaria are not within the scope of this paper. Reference is made only to those points which have been directly brought out by these experiments.

The refractory phase after a single formation of a chemical wheal (peptone, nettle) was regarded by Ebbecke as due to the exhaustion of the tissues. Török, Lehner and Urban believed it to be produced by the enhanced transportation of oxyhemoglobin and other inflammation-preventing substances to the area as a consequence of the increased blood supply. Goldscheider and Hahn [16] and Hoff [17] maintained that the abolition of the reaction capacity of the skin is brought about by the presence of latent edema, as in cardiac and renal edema.

The present observations show, first, that the erythematous zone becomes smaller and smaller after repeated injections. The explanation of this may be that less and less H-substance is produced, according to the recent views (Lewis) on the genesis of vascular reactions, or that the blood vessels become less and less responsive. Both theories correspond to well known physiologic processes (on the one hand, the changes of the chemicophysical properties of the cells in muscle and brain and, on the other hand, the diminution of the blood vessel reaction after repeated physical irritation from heat, light and cold).

4. The temporary cessation of wheal formation seems, according to my observations, to be a phenomenon independent of the nature of the urticariogenic substance, because the different substances produce also a desensitizing effect against one another. One receives the impression that the desensitization depends on the energy of the urticariogenic substance, but such a phenomenon is not regular, however, as is shown by morphine, for example. Accordingly, one has to presume that two factors are present at the same time; first, the wheal producing a desensitizing effect according to its dimension, and, second, another factor, X, based on a special quality of the urticariogenic substance but unrelated to its pharmacologic or chemical properties.

5. That the wheal formation is not an essential factor for the production of the refractory phase was shown by the experiment with the mixture of epinephrine and an urticariogenic substance. As in this experiment the desensitization was of shorter duration and less pronounced, two factors here again seem to be of importance: first, the urticariogenic substance itself and, second, the wheal formation, for in the experiment with the mixture it can also be assumed that latent wheal formation (by urticariogenic component) takes place, which could account for the desensitizing effect.

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THE BACTERIOPHAGE IN PYOGENIC INFECTIONS OF THE SKIN *

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The discovery by F. d'Herelle of the phenomenon of bacteriophagia in 1916 and his subsequent development of the subject are well known. In 1921, he [1] published the results of much careful work covering many phases of the field opened up by his original observations. Since then, many other investigators have reported on laboratory and clinical investigations confirming these observations.

Bacteriophagia may be defined as the dissolution of bacterial cells brought about by a filter passing principle which multiplies at the expense of the attacked bacteria and is therefore capable of exerting its lytic action through an indefinite number of serial passages.

Bacteriophage is prepared by suspending approximately 250 million young bacteria in alkaline (p_H 7.6) broth and adding a drop of lytic principle known to possess activity for the particular organism. Lysis is usually complete within from twelve to twenty-four hours when the lysate is passed through a Chamberland L 3 candle (to insure sterility).

Highly virulent polyvalent phages have been found for the staphylococcus and the dysentery bacillus. In both groups of organisms these already isolated and well studied phages may be effectively applied as therapeutic agents, for they have been shown to lyse practically all strains of their particular genus. In all other cases (with the colon bacillus, infection, etc.), one should make a preliminary susceptibility test with many races of phage. In the work reported here, an active polyvalent staphylococcus phage has been employed.

According to d'Herelle's book,[2] various bacteria have been found to be susceptible to bacteriophage action. They include *B. coli, B. dysenteriae* (Shiga), *B. paradysenteriae* (Hiss), *B. paradysenteriae* (Flexner), various intestinal bacilli, *B. gallinarum* and related organisms,

* Submitted for publication, March 29, 1929.

* From the Department of Dermatology, Stanford University School of Medicine.

* Read at the Fifty-Second Annual Meeting of the American Dermatological Association, San Francisco and Del Monte, Calif., July, 1929.

1. D'Herelle, F.: The Bacteriophage and Its Behavior, translated by George H. Smith, Baltimore, Williams & Wilkins, 1926, p. 269.

2. D'Herelle (footnote 1, pp. 242-269).

Pasteurella bovis, B. pestis, B. typhosus, B. paratyphosus A and B, *B. enteritidis, B. proteus, B. diphtheriae, Vibrio cholerae,* staphylococcus, streptococcus and various other pathogenic and nonpathogenic bacteria.

Gratia [3] first demonstrated a staphylococcus bacteriophage in 1921. In 1922, he [4] produced a polyvirulent staphylococcus phage that was effective against all strains (*albus, aureus* and *citreus*). D'Herelle found that about 100 strains of staphylococci isolated from different patients and also *Micrococcus tetragenus* were susceptible to this phage. Gratia treated about fifty patients with different staphylococcic infections. At first he tried injecting phage directly into the lesions, but found later that the results were just as good when the injection was given in another part of the body. The dosage varied from 0.5 to 3 cc. of filtered lysate. Usually only one injection was given, but in some cases a second dose was administered in twenty-four hours. The preparation was heated to 56 C. to destroy any bacteria surviving phage action. Painful erythematous and indurated areas developed at the site of injection and persisted for from twenty-four to thirty-six hours. A rise in temperature (40 C. [104 F.]) and a local inflammatory reaction in the lesions occurred. Gratia observed that the course of furunculosis, sycosis and subcutaneous abscesses was favorably influenced. None of his fifty cases had shown a recurrence in three months.

In 1921, Bruynoghe [5] reported his and Maisin's successful treatment with the staphylococcus phage in six cases of furunculosis.

Bastin,[6] following d'Herelle's suggestion, used suspensions that were not heated but simply filtered. He observed only slight local and no constitutional reactions and concluded that these phenomena resulted from changes in the albuminous substance produced by heating.

Nelson Barbosa [7] reported the successful treatment in cases of staphylococcus cystitis. Recovery (clinical and bacteriologic) occurred two or three days after the injection of from 0.5 to 1 cc. of a bacteriophage suspension.

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3. Gratia: Preliminary Report on a Staphylococcus Bacteriophage, Proc. Soc. Exper. Biol. & Med. **18**:217, 1921.

4. Gratia: La lyse transmissible du staphylocoque; Sa production ses applications thérapeutiques, Compt. rend. Soc. de biol. **86**:276, 1922.

5. Bruynoghe: Essais de thérapeutique au moyen du bacteriophage du staphylocoque, Compt. rend. Soc. de biol. **85**:1120, 1921.

6. Bastin, A. H. C. P.: Le phénomene de d'Herelle, considéré dans ses rapports avec la biologie générale, la pathogéne, la prophylaxie, et la thérapeutique des infections, Thèse, Lille, Leblanc & Durant, 1922, p. 112.

7. Barbosa, Nelson: Acção curativa do bacteriofago estaphylococcico, Brazil-méd. **37**:297, 1923.

Hauduroy [8] also recorded his successful results in treating staphylococcic infections.

Bazy [9] tried this form of therapy in "all types of localized pyogenic surgical infections." In some cases he injected the suspension directly into the lesions by a series of punctures encircling the sites of inflammation. In other cases, he injected it into some part of the body away from the lesions. He reported "excellent results" by both methods. To quote Bazy, "In all cases where the pathological condition involved only purely reactional phenomena, a rapid regression of the lesions and the *restitutio ad integrum* was witnessed. Whenever there was a tendency toward suppuration and necrosis, this developed rapidly, the abscesses matured better and more quickly, and the necrotic material was eliminated more rapidly. In short, recovery was accomplished after a very short delay." He differs with d'Herelle regarding the action of the preparation, the therapeutic effect of which, according to him, is due to the dissolved bacterial substances rather than to the bacteriophage itself.

Gougerot and Peyre [10] reported success in using bacteriophage suspensions locally in the treatment for sycosis. They first tried injecting the preparation subcutaneously, but their results were disappointing. Then they tried opening and injecting into each individual pustule (with a pipet) the bacteriophage, and applying the same suspension in moist compresses. This was done daily. After eight or ten treatments improvement was noticeable, and in two cases complete cure was noted.

Rice and Harvey [11] reported that in a series of fifty cases autogenous phage preparations have been found highly effective against *Staphylococcus aureus, S. albus, B. coli* and *B. pyocyaneus* when introduced into lesions or applied in compresses. They felt that polyvirulent stock phage also is effective.

Larkum,[12] of the Michigan Department of Health, recently reported favorable results from treatment with bacteriophage in sixty-six cases of furunculosis. In all but one of his cases, the condition responded well to the treatment. He used a polyvirulent strain of staphylobacteriophage which was found to produce lysis of 110 of 150 strains of staphylococcus.

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8. Hauduroy: Le bacteriophage de d'Herelle, Paris, Le Francois, 1925, p. 212.

9. Bazy, L.: Traitement des infections chirurgicales a staphylocoques par le bacteriophage antistaphylococcique, Compt. rend. Soc. de biol. **92**:485, 1925.

10. Gougerot and Peyre: Le bacteriophage dans le traitement des affections cutanée, Compt. rend. Soc. de biol. **91**:452, 1924.

11. Rice and Harvey: Therapeutic Use of Bacteriophage of Suppurative Conditions, J. Lab. & Clin. Med. **14**:1 (Oct.) 1928.

12. Larkum, Newton W.: Bacteriophage in the Treatment of Furunculosis, J. Michigan State M. Soc. **27**:106 (Feb.) 1928.

Immediate and latent immunity to avian typhosus and barbone (a septicemic disease of the buffalo) and bacillary dysentery have been produced by d'Herelle.[13] This work has been confirmed by a number of investigators, and definite failures are reported by other authors. This is discussed in chapter 5 of d'Herelle's book.

A brief review of the therapeutic results in various infections has been presented by E. W. Schultz, professor of bacteriology at Stanford University, and should be read by all interested in the subject.[14]

In the closing chapter of his book,[1] d'Herelle concluded that: "For certain diseases—bacillary dysentery, staphylococcus infections and colon bacillus infections, phagotherapy is becoming an established procedure and many authors consider it specific. I hope that this will presently be true for plague."

The following recommendations are made by d'Herelle for the proper carrying out of bacteriophage treatment:

> First, one should use a polyvirulent suspension, which should be filtered and never heated.
>
> For furunculosis and folliculitis, the dose is 1 cc. subcutaneously (preferably under the skin of the abdomen). The injection should be repeated only once after an interval of not longer than forty-eight hours.
>
> For local abscesses, from 1 to 2 cc. is injected into the immediate vicinity of and around the lesion. If it is possible to make the injection directly into the lesion, from 0.25 to 0.5 cc. of the preparation should be used.
>
> For sycosis, the technic of Gougerot and Peyre is employed (injections into each pustule and compresses of bacteriophage suspensions over all the areas).

From Oct. 22 to 26, 1928, Professor d'Herelle delivered the series of Lane lectures at Stanford University School of Medicine. Since then, the department of bacteriology of Stanford University, under the direction of Prof. E. W. Schultz and Dr. Albert P. Krueger, has been preparing "phage" for experimental clinical use by certain authorized physicians. This treatment is being carried out in the various departments at Stanford on pyogenic infections of the skin, in wound infections, cases of sinusitis, urinary infections and osteomyelitis, with varying results (some of them encouraging and some failures). Its successful use in these conditions and also in cases of bacillary dysentery, cholera, bubonic plague and typhoid is fully discussed in d'Herelle's book.[1]

In the department of dermatology at Stanford University and in private practice, this form of therapy has been applied in a series of selected cases of pyogenic infections of the skin.

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13. D'Herelle (footnote 1, pp. 510-539).

14. Schultz, E. W.: The Bacteriophage: Its Prophylactic and Therapeutic Value, California & West. Med. **27**:481 (Oct.) 1927.

The following case records are in the nature of a preliminary report, for this work has been organized only recently. In only three of these cases (8, 9 and 10) has the phage been typed, that is, cultures have been made and phage suspensions capable of completely lysing the causal bacteria, as demonstrated by in vitro tests, prepared. A polyvalent staphylococcus bacteriophage has been used in most of these cases. In the future, under Professor Schultz's direction, the phage will be typed in all cases and the results reported.

REPORT OF CASES

CASE 1.—Mrs. S. J. F., a housewife, aged 32, has had acne vulgaris for many years. For the past four months she had presented on the chin and in the region of the mouth numerous indolent deep "cystic" pustules. She was underweight, anemic and nervous. Six weeks before presentation, the tonsils were removed by Dr. Wallace Smith on account of chronic infection there and frequent colds. The acne did not improve, but grew worse.

On Oct. 16, 1928, 2 cc. of staphylococcus (polyvalent) bacteriophage was injected subcutaneously into the outer aspect of the right arm. Frequent applications of a carbon tetrachloride cleansing lotion and a powder consisting of phenol, salicylic acid and zinc oxide were prescribed.

On October 17, the site of injection was erythematous, slightly edematous, warm and painful. The acne lesions were unchanged, and the temperature was normal.

On October 18, the local reaction caused by the injection had subsided. The acne lesions had improved greatly in appearance.

On October 19, a remarkable subsidence of most of the acne lesions had occurred. One large soft papule was incised, and no pus was found, only blood. Three cubic centimeters of the same phage was injected into the outer aspect of the left arm.

On October 20, the temperature was normal, but the previous evening the patient experienced "general aching" in the limbs, and the site of the injection was edematous, erythematous and painful.

The next day this had subsided. The acne lesions were disappearing rapidly.

On October 25, the patient was almost well. The induration marking the sites of the original lesions had largely disappeared.

On November 5, there were no lesions. On account of the dryness and pigmentation of the skin, an ointment containing salicylic acid and phenol was prescribed.

On November 15, the skin was smooth. There was no pigmentation. The patient promised to report promptly if any lesions should develop.

On March 15, 1929, she was entirely well.

CASE 2.—M. R. J., Jr., a student at Stanford University, aged 17, in good general condition, presented numerous small and large deep (cystic) pustules and many deep cicatrices all over the upper and lower parts of the back, the upper part of the chest anteriorly and the back of the neck. He had been having these lesions constantly for more than two years.

From June, 1927, to Oct. 20, 1928, under the usual external and internal medication, more or less unsuccessful regulation of the diet and roentgen therapy, the acne at times improved and then grew worse. The patient's college and social duties often interrupted his treatment. Frequently, he would indulge in forbidden

foods, with unfavorable results. Whenever he carried out his treatment steadily for two or three weeks, the condition of the skin improved, but deep indolent pustules still kept appearing.

On Nov. 10, 1928, 1 cc. of a polyvalent staphylococcus bacteriophage was injected subcutaneously.

On November 12, the old lesions had flattened down perceptibly, and there were no new pustules. Three cubic centimeters of the same "phage" was injected.

On November 14, the acne lesions were steadily subsiding. The site of injection was inflamed and painful for a day, and the patient had had a sharp constitutional reaction (fever, chills and general aching) the day of the inoculation.

On November 28, no new pustules had appeared, but four days after the last injection several large papules were found on the upper part of the back and on the shoulders. These did not develop into pustules, as was the rule with such lesions formerly.

On December 5, a few new papules kept appearing, but none became pustules.

Up to the present time the patient has made five visits, and only rarely has anything like a pustule appeared, although he continued to have large papules and occasionally urticaria (due to indiscretions in diet). Several indolent papules have been incised at different times, and usually nothing but blood and serum has been evacuated. A nodule has rarely yielded a small amount of thick pus, the contents having more the appearance of sebaceous material.

Case 3.—A watchmaker, aged 21, in good general condition, had typical furuncles on the hands, forearms and buttocks of more than one week's duration. The blood counts, Wassermann reaction and urinalysis all gave normal results. The following treatment was given:

On Jan. 9, 1929, 1 cc. of polyvalent staphylococcus bacteriophage was injected subcutaneously.

On January 12, some improvement was noted. Two cubic centimeters of the same phage was injected.

On January 16, the condition was much better. Two cubic centimeters of the same phage was injected.

On January 19, the patient was almost well. Two cubic centimeters of the same phage was injected. One month after the last injection the patient was observed to be entirely well, having had no new lesions since the last injection. (A 5 per cent ammoniated mercury ointment applied locally was the only other treatment given.)

Case 4.—L. R., a laborer, aged 21, in good physical condition, presented several furuncles in the bearded region of the face, of several weeks' duration. He had had a similar attack one year previously which was promptly relieved by local treatment only. Since then, there had been several recurrences. Examination of the blood and urine gave negative results.

On Nov. 7, 1928, 1 cc. of polyvalent staphylococcus bacteriophage was injected subcutaneously.

On November 10 and 14, respectively, 2 cc. of the same phage was injected. After the last injection recovery was complete, and two months later the patient remained well.

Case 5.—A. P., a janitor, aged 59, had furunculosis of over a week's duration involving the hands and forearms. Gentian violet (1 per cent solution) and 5 per cent ammoniated mercury had been applied without much effect.

On Nov. 23, 1928, an injection of 1 cc. of the polyvalent staphylococcus bacteriophage was given.

On November 26, 2 cc. of the same phage was injected, and this dose was repeated on December 6, 10 and 14. Great improvement occurred soon after the second injection, and two months later the patient still was free from lesions.

CASE 6.—C. D., a laborer, aged 34, had several large furuncles on the thighs. He had been having these lesions constantly for two years in spite of the usual surgical treatment. The blood count was as follows: red blood cells, 5,130,000; white blood cells, 12,800; hemoglobin, 65 per cent; polymorphonuclears, 75 per cent; lymphocytes, 21 per cent; eosinophils, 2 per cent.

The urine showed no dextrose or albumin. The patient was given 1 cc. of the polyvalent staphylococcus bacteriophage on Dec. 19, 1928, and 2 cc. of the same on Dec. 22, and on Jan. 3, 6 and 9, 1929, respectively. Shortly after the second injection marked improvement was noted, and at the time of the last injection he was almost well. This paper was written two months after the last visit.

CASE 7.—J. W., a press feeder, aged 25, had furuncles on his face and arms of several weeks' duration. He received the usual local surgical treatment with out results. The urine showed no dextrose or albumin.

On Jan. 3, 1929, 1 cc. of the phage was injected.

On January 6, 10 and 12, 2 cc. of the same was injected. After the second treatment great improvement was observed, and when the patient received the third injection he was entirely well. Two months later, he was still well.

CASE 8.—W. C., a university student, aged 23, had acne vulgaris of seven years' duration. He had had a great deal of the usual treatment with only temporarily beneficial results. He was fairly well developed, of sedentary habits, with a history of chronic constipation and poor dietary regulation (excess of carbohydrates). The acne was mainly of the pustular type, involving the forehead, cheeks and upper part of the trunk. He had a seborrheal skin.

Bacteriologic examination of pus from several lesions revealed a pure culture of *Staphylococcus aureus*. This was found to be completely lysed by two antistaphylococcus phages.

Three injections of 1, 3 and 3 cc., respectively, were given at intervals of twenty-four hours. There were slight local reactions at the sites of injection and no constitutional symptoms. On the fifth day after the first injection, the pustular elements were undergoing marked regression. Within another three days the circumference of each papule was distinctly smaller, and no pustules remained. Since then the condition has remained satisfactory, as far as the acne is concerned.

CASE 9.—L. T., an American student, aged 22, had had seborrheic dermatitis and acne vulgaris of the pustular type for six years. He had received sporadic treatment of various sorts for the past five years (lotions, roentgen treatments, etc.). There was some improvement after dietary regulation and roentgen therapy, though it was not marked. Recurrence of the pustular lesions always followed the least dietary indiscretions. The patient was well built and active and in excellent general health. The skin was slightly thicker than normal; marked seborrheic dermatitis and numerous small pustules surrounded by erythematous areolas over the face and neck were present. There was moderate nonpustular acne over the upper part of the back.

Two pustules were incised, and cultures yielded pure cultures of *Staphylococcus aureus*. This organism was completely lysed by an antistaphylococcus bacteriophage.

Three subcutaneous injections of 2 cc. each were given, at twenty-four hour intervals. Slight erythema occurred at the site of injection, and the temperature

was 99.3 F. after the third injection. All pustules had subsided two days after the last injection, leaving only papules. No recurrences have been noted since. There was little, if any, immediate effect on the nonpustular lesions which had responded to subsequent local measures. The patient remains in good condition.

CASE 10.—L. S., an American high school student, aged 16, had had chronic furunculosis of the neck, cheeks and buttocks for one and a half years. Dietary regulation and autogenous vaccine begun sixteen months before presentation produced some improvement, but there were three recurrences of acute furunculosis during the six months before phage therapy was begun. The patient was seen during an acute exacerbation. He was fairly well developed and well nourished, with thick skin and seborrheic dermatitis; there were three moderately large, fluctuating furuncles, already suppurating, on the back of the neck and one smaller, nonfluctuant boil on the right cheek. There were also several scars and fibrosed areas from previous lesions.

Culture from one incised boil yielded a strain of *Staphylococcus aureus* completely lysed by three races of antistaphylococcus bacteriophage.

One of the three furuncles on the back of the neck was incised to obtain a culture of the causal organism. The other lesions were not treated by any local measures. Three subcutaneous injections of 3 cc. each were given at twenty-four hour intervals with only slight local reaction at the site of injection. About twelve hours after the first injection, the two unincised furuncles on the neck became more turgid and painful and opened spontaneously, draining considerable fluid pus. On the day after the second subcutaneous injection, the lesion on the cheek underwent rapid regression, while the three draining furuncles on the neck were practically dry. At the time the patient presented himself for the third injection the dressing was dry, and healing had progressed in all the infected areas. No further visits were required. There have been no recurrences since the foregoing episode (ten months).

The seborrheic dermatitis is being treated at present.

Additional Cases (Incomplete Records).—In two cases of chronic sycosis vulgaris and one of severe carbuncle of the neck in which phage was used by the physicians, detailed reports have not yet been supplied. As the reported end-results were completely negative, it is felt that these cases should be mentioned here. It is hoped that by the time this paper is read full reports will be available. A possible explanation of failure in these three cases lies in the fact that the phage was not injected in the vicinity of the lesions. Gougerot[10] reported successful results when the phage was injected into each lesion.

COMMENT

In all but three of the cases reported (8, 9 and 10) polyvirulent staphylococcus phages were used. All of the injections were given subcutaneously at a place remote from the location of the lesions.

It will be seen that the encouraging experiences in cases 1, 2, 4, 6, 7, 8 and 9 were similar to the favorable results reported by others. There were no local or general reactions except those noted in cases 1 and 2; they are impossible to explain at this time, for the injections were given under proper aseptic conditions, and the phage was not heated.

In cases 3 and 5 the condition was of too recent origin to justify an opinion as to the efficacy of the treatment. Certainly the patients

were not made worse by phage therapy and improvement and recovery were definite.

In cases 8, 9 and 10 the phages were "typed"; that is, cultures made from pus from the lesions were tested with several races of staphylococcus phage, and the phage that was found to have the maximum lysing effect on the same was used therapeutically. This, of course, is the more scientific method and is now being carried out in all cases that will be reported later.

Although more than two injections were given in eight of the cases, it was observed that in all improvement was seen after the second injection. The extra injections apparently did no harm.

CONCLUSIONS

From recent experiences with a small number of carefully selected and observed cases of acne vulgaris (pustular type) and furunculosis, it is felt that good results may be expected from this form of therapy. Until several hundred such cases are studied, however, the question of variations in results reported by others and that of artificial immunity will remain unsettled.

ABSTRACT OF DISCUSSION

DR. E. D. CRUTCHFIELD, San Antonio, Texas: I enjoyed Dr. Alderson's paper, which certainly brought out new concepts in immunology. Several months ago I procured a bacteriophage from Larkin of the University of Michigan, with which, in a series of cases, I obtained results similar to those reported. For some reason, these results were not constant. It was felt that something had happened to the bacteriophage. A new phage was then developed, and the results were still indefinite. I wonder whether Dr. Alderson has had the same experience, and how he obtained the polyvalent phage for all these organisms. My results differed somewhat from his. In one case of dermatitis vegetans, I felt that the patient was relieved by injection of bacteriophage. However, I got such poor results in deep furuncles that I decided that the bacteriophage worked better in superficial lesions. By injection into furuncles I obtained no results, and by topical applications I got poor and unsatisfactory results in about fifteen or twenty cases of furunculosis. I have wondered also whether or not the immune bodies produced in the skin may not explain the difference in results in treating deep and superficial infections.

DR. ALDERSON: I should like to ask Dr. Crutchfield whether he has made cultures and tested them against various phages. We are "typing" all our cases now.

DR. CRUTCHFIELD: I have in the late instances.

DR. ALDERSON: We are getting better results when we do that. Professor Schultz has on hand all the phages that have been found potent, including the well known Gratia phage. I should like to know whether Dr. Crutchfield gave more than three injections.

DR. CRUTCHFIELD: No.

DR. ALDERSON: It is known that in some cases something like an antiphage develops. Of course, we have failures, as I mentioned, but some of the successful results are so striking that we feel we have something that is worth while working on for another year or two.

NODAL FEVER OF LENDON

(EMBOLIC DERMATITIS) *

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This is the report of a case in which nodose lesions like those of erythema nodosum occurred in the skin of the breasts of a woman, aged 26.

REPORT OF A CASE

Mrs. S. C., aged 26, seen May 1, 1929, in the practice of Dr. M. Edward Davis, complained of painful nodose lesions on the breasts, chest and upper part of the arms of two days' duration. For a few days before the outbreak, she had been conscious of a "peculiar feeling of discomfort" in the breasts. There was no actual pain, burning, itching or tenderness, and the discomfort was very slight, not enough to cause her to seek advice. She had been delivered four months before and was feeding her baby from the breast, so that not unnaturally she attributed the discomfort to congestion. In other respects, her health was good. There was no fever, sore throat, aching of the joints or other complaints.

The first lesion appeared on the right breast, in line with the nipple and about 2 inches (5 cm.) above it. It was painful and very tender when touched. A few hours later, two more lesions appeared on the same breast. They were likewise tender to touch. When seen the next day, she had ten lesions distributed over the sternum, both mammary glands, and the adjacent surfaces of the upper part of the arms. She had slight pain, and the solitary lesion over the sternum was exquisitely tender when pressed. The lesions in the soft tissues were not so tender. The nodes were 1 or 2 cm. in diameter, were slightly oval and appeared to be situated deeply in the skin; on the legs, they would have passed for erythema nodosum. As sometimes happens with erythema nodosum, a surgeon who saw her first advised incisions to stop the spread of the infection. The lesions were violaceous, the newer ones being a slightly brighter red. The patient was up and about, with a temperature of 99.2 F. There was no evidence of rheumatic infection. Signs of focal infection were not apparent, and the patient was comfortable. There had not been any previous attack. A sister had died ten years before of pulmonary tuberculosis, but the other members in the family, of whom there were four, were apparently well.

It was thought wise because of the history of tuberculosis in a sister, and because the patient had been recently confined, to place her in the hospital and to institute a careful search for possible foci of infection.

She entered the hospital with a temperature of 99.2 F. She was put to bed, and no medication was ordered. Examination of the blood showed: hemoglobin, 85 per cent; red blood cells, 5,460,000; white blood cells, 10,700; neutrophils, 68 per cent; small lymphocytes, 18 per cent; large lymphocytes, 12 per cent, and transitionals, 2 per cent.

A blood culture was sterile. The urine was normal. Two new lesions appeared that day, but on the fourth day following all the lesions were gone. In their evolution, they passed through all the changes seen in lesions of typical erythema

* Submitted for publication, Nov. 26, 1929.

nodosum. The outlines were not well defined, the borders merging gradually into the adjacent tissues. Some of the lesions became slightly boggy; there was no desquamation, and no scars remained.

Physical and roentgenologic examination did not reveal any pathologic condition in the chest. The patient was repeatedly examined for any hidden foci of infection, but none was found. Another blood culture was sterile. Four days after entering the hospital, the patient was afebrile, and the white blood cell count was normal. A tuberculin test was not done. She was discharged after a few days, and to the time of this report her course has been uneventful.

COMMENT

One hesitates to classify a condition as an embolic process without being able to demonstrate a focus of infection. Unfortunately, however, this failure occurs only too frequently.

The place of these conditions in medicine is receiving considerable attention of late. The older view that these nodose eruptions are in some way connected with rheumatic fever has lost ground in favor of Lendon's view that the rash is that of an acute specific infectious disease which he designates "nodal fever." Nodal fever is described as a mildly infectious disease, more common in the spring and autumn, with an incubation period of about fourteen days. Prodromes may be mild or intense, the exanthem is precise and uniform, and convalescence, though usually uneventful, may be fraught with danger. The infection more frequently occurs in young women. There is a growing tendency on the part of many workers to regard the condition as being associated with tuberculosis. The experimental evidence for this view is scant, and it has been suggested that these nodose conditions may well be a specific infectious disease, with a particular likelihood that in the postfebrile debility tuberculosis may be established. It was this possibility that led us to proceed so cautiously with our patient. Nodose lesions with erythema multiforme are encountered, and they occur also from infarcts in septicemia.

SUMMARY

In the case reported here of nodal lesions in the skin of the chest, while it seems likely that they were the results of septic infarcts, no focus of infection could be demonstrated. The patient was a healthy young woman, who had been delivered four months previously. There have not been any recurrences or sequelae. The case is offered as an example of Lendon's nodal fever in a mild form.

7 West Madison Street.

SOME RECENT ASPECTS OF INTERNATIONAL COOPERATION IN SYPHILOLOGIC RESEARCH

A SUMMARY OF ACTIVITIES SPONSORED BY THE LEAGUE OF NATIONS *

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Under the aegis of the Health Committee of the League of Nations a series of public health activities of great importance to modern syphilology has been in process of development since 1921. In that year a plan for the conduct of comparative studies of modern serodiagnostic tests for syphilis was adopted, and in 1922 the first reports, covering the work carried out in eight European State Laboratories, were made at a conference in Paris. In 1923, the work was continued by these laboratories, but the results could not apparently be brought into any convincing form of agreement so long as the individual laboratories examined their own material. Accordingly, the Danish Serum Institute undertook to supply all the material for testing by the various laboratories interested in the work, including those of Berlin, Brussels, Frankfurt-am-Main, Heidelberg, Copenhagen, London, Oxford and Vienna. Even this attempt to secure an adequate comparison of a variety of serologic procedures for the diagnosis of syphilis was not wholly successful. It was accordingly decided to call an international conference of laboratory investigators, to be held in Copenhagen at the Danish Serum Institute in November-December, 1923. The technic of this conference consisted in the testing of 536 samples of blood by twelve different methods: eight Wassermann technics, two Meinecke procedures, one Sachs-Georgi and one Sigma technic. The conference concluded that while, at that day, the Wassermann procedures yielded the larger proportion of positive results for syphilis, the precipitation tests, though less sensitive, yielded enough positive results in syphilitic cases when the Wassermann reaction was negative to justify the use of precipitation tests to supplement the routine use of the Wassermann type of procedure.

The years from 1923 to 1928 were signalized by a marked advance in the technic of precipitation tests throughout the world, with respect to both their sensitivity and their specificity. Accordingly, in response to a number of requests, the Health Committee of the League of Nations in June, 1928, held a second Serologic Conference at Copenhagen. The conclusions of this conference as now published are not only a notable

* Submitted for publication, Sept. 25, 1929.

advance in knowledge of a most important group of diagnostic procedures, but reveal the development through the successive stages enumerated of a genuine technic of international cooperative investigation.

The success of the Serologic Conferences of 1923 and 1928 may conceivably have served as the inspiration for the calling of yet a third conference, this time on a clinical topic. Coincidently with the meeting of the Serologic Conference at Copenhagen in June, 1928, the Health Committee of the League of Nations held a series of informal pourparlers between representatives of Great Britain, Germany, France, the Scandinavian countries and the United States, with reference to a plan for international investigation of the methods and results of the present-day treatment for syphilis. In his opening remarks, Professor Rasch directed attention to the general impression afforded by the entire field; that of cross-purposes, variant technics and results apparently small out of all proportion to the effort expended. As a result of this preliminary discussion, a Committee of Experts representing the countries named was invited to assemble at Geneva in October, 1929, and to draft a plan and form of inquiry into the treatment for syphilis. Supported by the important clinical groups in this field in the various countries concerned, it is hoped that a sufficient mass of material can ultimately be compiled and analyzed to form the basis for concepts of treatment in syphilis which may have international validity and acceptance.

The conclusions at the Serologic Conference of June, 1928, may first be summarized. It must be a source of lasting satisfaction to Americans that in this conference the work of Kahn, who was present in person, earned the distinguished position accorded it; and it must be a source of lasting regret that the most widely known American investigator of complement-fixation procedures, Kolmer, while invited to attend, was prevented from being present. The conference was therefore unable to contribute to the comparative evaluation of the two most popular American procedures: the Kolmer modification of the Wassermann reaction and the Kahn precipitation test.

The conference of 1928 was attended by a number of eminent serologists from seventeen countries. Fifteen different methods employed for the serodiagnosis of syphilis were compared, including seven different modifications of the Wassermann reaction and eight different flocculation methods (Kahn, Murata, Meinicke, Müller, Sachs-Georgi, Vernes and Sigma). Each participant employed only one method. Ten of them were carried out by their authors. Nine hundred and forty-four samples of blood and 122 samples of spinal fluid were examined. Some of these came from Danish hospitals, and some were sent to Copenhagen by air mail from other European cities, such as Berlin,

Hamburg, London, Paris and Vienna. The clinical diagnosis of the serums was not made known to the investigators until they had given the results of their tests. In cases in which the clinical diagnosis and the serologic observations did not agree, the test was repeated and the patients were submitted to further thorough clinical and specialist examinations.

Of the 944 serums tested, 502 were derived from cases known with certainty to be syphilitic both by treatment and from the case history; 442 serums came from patients without any clinical indications of syphilis. The detailed clinical diagnoses in the two groups of patients are given in table 1.

The detailed results are shown in tables 2 and 3, in which the different serologic methods are arranged according to the degree of sensitiveness and specificity which the investigation showed them to possess. Doubtful (±) reactions are left out of account. In the two tables,

TABLE 1.—*Detailed Clinical Diagnosis in the Two Groups of Patients*

Syphilitic Cases		Nonsyphilitic Cases	
Primary syphilis	20	Gonorrhea	101
Secondary syphilis	25	Pregnancy	75
Tertiary syphilis	62	Tuberculosis	61
Latent syphilis	300	Tumors	27
Congenital syphilis	10	Lupus vulgaris	25
Tabes	30	Dementia praecox	24
Dementia paralytica	55	Psoriasis	12
		Ulcus molle	11
Total	502	Scarlatina	8
		Miscellaneous	99
		Total	443

seven serums that were described in the original report as doubtful have been omitted. The details of these cases are to be found in the original report.[1]

Two series of examinations of the spinal fluid were conducted. The first, in which all the serologists participated, while numbering only sixty-seven specimens, seemed to indicate, allowing for the small material, that the best results were obtained with the Harrison-Wyler technic of the British Ministry of Health (Medical Research Council No. 1), and the second best results with the Müller clotting and the Kahn tests. A subsequent comparison, conducted by Kahn, Harrison and Wyler in London following the Conference, in which 565 samples of fluid were examined, 508 of them from syphilitic subjects, indicated that when the fluid is clear, the Kahn is superior to the Harrison-Weyler Wassermann, while the reverse is true if the fluid is cloudy or turbid. Study of the nonagreements indicated that the two tests cannot yet completely replace

1. Report of the Second Laboratory Conference held at Copenhagen, May 21 to June 4, 1928, C. H. 726, pp. 26 and 27.

TABLE 2.—*Methods Classified According to Sensitivity*

Rank in Series	Methods Based on Wassermann Principles	Flocculation Methods	Tests Performed by	Percentage of Positive Reactions in Syphilitic Cases	Percentage of Positive Reactions in Nonsyphilitic Cases
1		Müller's clotting test	R. Muller, Vienna	63.5	0.2
2		Kahn	R. L. Kahn, Lansing (U. S. A.)	61.1	0
3		Kahn	H. Boas, Copenhagen	58.5	0.7
4	Active		E. Debains, Paris	53.0	10.4
5	Synoptic		E. Jacobsthal, Hamburg	52.8	6.7
6	Original		R. Otto and G. Blumenthal, Berlin	51.8	5.5
7		Murata	M. Nagayo and K. Nogechi	51.3	0.5
8		Citochol reaction Sachs-Georgi	H. Sachs and E. Witebsky, Heidelberg	51.2	0
9		Sigma reaction	K. Norel, Copenhagen	51.2	1.4
10		Meinicke's turbidity test	E. Meinicke Ambrock, Hagen, Westphalia	49.0	2.1
11	Original		D. Pavlovitsch, Belgrade	43.9	1.4
12		Lentochol reaction (Sachs-Georgi)	H. Sachs and E. Witebsky, Heidelberg	41.9	0
13	Medical Research Council method, no. 1		L. W. Harrison and E. Wyler, London	41.8	0
14	MacIntosh-Fildes		S. Sierakowski, Warsaw	38.8	0
15		Vernes' sypilimetric method	A. Vernes and H. Bricq, Paris	38.4	0.5
16	Modification carried out by de Blasi		D. de Blasi, Naples	28.2	3.3

TABLE 3.—*Methods Classified According to Specificity*

Rank in Specificity Series	Rank in Sensitivity Series	Methods Based on Wassermann Principles	Flocculation Tests	Percentage of Positive Reactions in Syphilitic Cases	Percentage of Positive Reactions in Nonsyphilitic Cases
1	2		Kahn	61.1	0
2	8		Sachs-Georgi Cito	51.2	0
3	12		Sachs-Georgi Lento	41.9	0
4	13	Wassermann Reaction, Medical Research Council No. 1		41.8	0
5	14	Wassermann, McIntosh-Fildes		38.8	0
6	1		Müller's clotting test	63.5	0.2
7	7		Murata	51.3	0.5
8	15		Vernes	38.4	0.5
9	3		Kahn-Boas	58.5	0.7
10	9		Sigma	51.2	1.4
11		Wassermann reaction, original method		43.9	1.4
12	10		Meinicke's turbidity test	49.0	2.1
13	16	Wassermann de Blasi		28.2	3.3
14	6	Wassermann, original method		51.8	5.5
15	5	Wassermann, synoptic method		52.8	6.7
16		Wassermann, active method		53.0	10.4

one another, but must be regarded as complementary if the best result is to be obtained.

From the syphilologic standpoint, attention should be specially called to the fact that every effort was made to meet all the requirements for a valid judgment as to the worth of the serologic procedures compared. The clinical material from which the specimens of blood and spinal fluid in the Copenhagen Conference were drawn was rigidly controlled from the clinical standpoint by the foremost syphilis clinics of Europe. This was no mere interlaboratory or intralaboratory technical comparison such as has attained such unwarranted popularity in this country during the serologic skirmishes of the last half decade, but a bona fide comparison of the test procedures with the clinical facts. Even the records of the seven doubtful cases were examined by the Committee of Experts at Geneva the following October, before publication of the results. The tests were performed in all cases by their ablest exponents, usually the originator himself. Every facility was provided. With commendable conservatism as well as diplomatic good sense, the members of the Conference, after appraising the results, declined to designate any test as "the best," pointing out wisely that the merit of a diagnostic test is dependent on a variety of factors that must be determined for the individual laboratory service or clinic—not the least of which are convenience and expense. None the less, certain conclusions stand out from the work of the conference with a definiteness that deserves world-wide attention. Foremost of these conclusions is the evident tremendous advance in specificity and sensitivity score by the precipitation tests over the complement-fixation tests for syphilis in the last few years. The Kahn test and the Müller clotting test entirely outclass in sensitivity the Wassermann procedures considered, apparently without loss of specificity. On the score of specificity the Kahn and the Sachs-Georgi lead the nearest Wassermann competitor, the British Medical Research Council Method No. 1, by a substantial margin. Taken all in all, the performance of the Kahn test is outstanding and places it as among the best, if not the best, serodiagnostic procedure in the syphilology of the present day. Again it must be said with regret that circumstances prevented Kolmer from being present at so genuine a trial of strength. The conference wisely endorsed a conclusion that will appeal to the majority of syphilologists who must interpret the disease to the patient in the clinic—that for the time being more than one procedure, and preferably one complement-fixation and one precipitation test, be performed on every blood that is being studied for evidence of the presence of syphilis. The large margin of nonspecific reactions, ranging from 1.4 to 10.4 per cent, obtained with Wassermann modifications that do not differ essentially from tests in common and

exclusive use in the laboratories of this country, indicates that many patients are today being sentenced, the world over, to treatment for syphilis on insufficient and untrustworthy evidence.

It is to be hoped that the third Serologic Conference, whenever it may be called, will include in its agenda some of the recent notable simplifications of precipitation procedure that have been developed in this country, such as the Kline slide test on blood drawn from finger puncture and the microprecipitation tests on chancre fluid which may be substituted for the relatively impracticable dark field.

The work of the Committee of Experts on Syphilis and Cognate Subjects appointed to plan a clinical survey of the treatment for syphilis, begun in Geneva in October, 1928, cannot be reported on at this time in terms of results; but a statement of aims and methods may be of interest. The membership included Rajchman, Director of the Health Committee, League of Nations; Rasch, Copenhagen; Madsen, Copenhagen (Serum Institute); Harrison, British Ministry of Health; Querat, French Society for Combatting Venereal Disease; Stokes, United States Public Health Service, with Jadassohn (Breslau), the most eminent of European clinical syphilologists, as chairman. The committee has drawn up a case protocol and has asked the cooperation of a number of clinics in the countries represented, in the transfer of their case history records to this form. The case protocols thus prepared will be collected by the Health Committee for study. It was agreed that the investigation should limit itself to the early and latent phases of syphilis and embrace the consideration of facts connected with clinical and serologic response and cure, relapse and progress of the disease in its early stages under all methods of treatment in use at the present day, except fever therapy. The material is restricted to cases that have been under observation in the participating clinics for not less than six months. The protocols or case record forms will be evaluated by a central statistical bureau in connection with the Health Organization of the League at Geneva. As high as 100 clinics are participating, and the number of records examined will mount into the thousands. As in the case of the Serologic Conference, only experience with the work will develop an adequate technic of investigation—and it is hoped that over a period of years, if support can be continued, many phases of the treatment for syphilis can be thus cooperatively studied on a large scale.

In the United States, the League investigation is being carried on with the cooperation of the United States Public Health Service and certain private resources made available for the purpose through the organization of the Committee on Research in Syphilis, Inc. The American investigation, while like the European, limited to early syphilis, endeavors to go into details which it is impossible to undertake at this

time in a study on the scale of the League investigation. Five American syphilologic clinics have been organized into a cooperative unit to supply the American share of material for this study, and from their fuller protocols the material for the League Research drawn from this country will be abstracted. It is not expected that there will be any important presentation of results within a year. It is to be hoped that this most recent venture of the Health Committee of the League into the field of syphilologic therapeutic research will be as productive of stimulating and important conclusions as was its predecessor in the field of serodiagnosis.

DISCRETE KERATODERMA OF THE DORSUM OF THE HANDS

A PROBABLY UNRECOGNIZED ENTITY *

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In the past several years, I have seen three patients presenting discrete hyperkeratotic patches on the dorsum and lateral surfaces of the hands, about which no satisfactory description seems to appear in the literature. From correspondence with physicians of large experience, it appears that these cases are not uncommon and that they may be representatives of an unrecognized entity. My search through the literature, fairly thorough as far back as 1919, but incomplete for the period before that, does not reveal any article that bears directly on these cases. Probably they have passed for manifestations of one of the more common disorders of the skin but I think that such a ready assumption will not bear close scrutiny.

Briefly, the lesions appear only on the back or lateral surfaces of the hands, bilaterally but not symmetrically, as discrete, slightly raised patches varying in color. The predominant color is yellow, but they are sometimes skin colored, gray, brown or dusky red. Their surfaces are sometimes smooth and shiny or slightly roughened and dull. Usually, the surface markings are obliterated. Their borders are fairly well, but not sharply, defined. In the main, they more closely resemble callositas than any other dermal manifestation. They vary from 4 to 5 mm. to several centimeters in diameter and from quadrangular to circular. They occasion no subjective symptoms. In my cases they have persisted practically without change for long periods and have proved recalcitrant to treatment.

Whether or not these cases are representatives of a hitherto undescribed entity, as I believe they are, must remain sub judice. But even if they are not, it would appear that a discussion of them at this time would not be fruitless, since the literature on them is apparently scarce, and standard texts on dermatology contain nothing helpful in regard to their clinical features, classification or treatment.

REPORT OF CASES

CASE 1.—*History.*—Mr. H., aged 35, an automobile salesman, was first seen on Nov. 8, 1923, with a disturbance of the skin of one and one-half years' duration. It involved only the back of the hands and was unaccompanied by any

* Submitted for publication, July 30, 1929.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 10, 1929.

other cutaneous disease. He said that it began with small firm points which gradually enlarged and became somewhat roughened. The increase in the size of the lesions was slow, and in the previous several months there had been no appreciable change in them. They did not itch or cause any other subjective sensations. In fact, they gave him no concern, and were it not for an occasional comment by an acquaintance, he would not have consulted a physician. The only other skin eruption that he recalled having had was a number of common warts on the back of the hands about five years previously. After remaining for a year, these disappeared spontaneously.

He had never been seriously sick, and his general health and functions were normal. He was married, but neither his wife nor any of his immediate family had any skin disease so far as he knew. He said that he had not had venereal disease.

A general physical examination showed a robust man with no grossly detectable visceral abnormalities. The results of the usual routine laboratory examinations

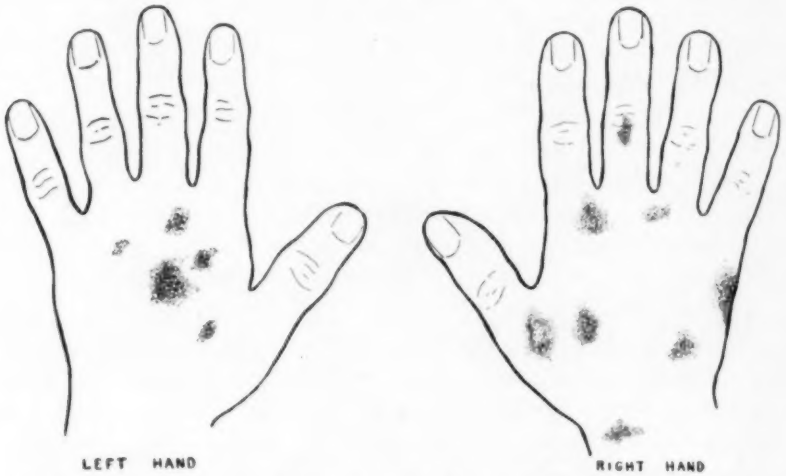

Fig. 1.—The location, relative size and shape of the lesions in case 1.

were negative, except the Wassermann, which gave a 2 plus reaction, and on repetition after a provocative injection, a 3 plus reaction resulted.

Skin Manifestations.—The lesions were present on the back of the hands, except that one was situated on the dorsum of the right wrist and one extended to the external lateral surface of the same hand (fig. 1). There were eight lesions on the right hand and five on the left. They were raised very slightly above the level of the surrounding skin. They varied in shape, the smaller being more angular than the larger. All were isolated. They ranged from 4 mm. to 2.5 cm. in their longest diameter. The smallest lesion somewhat resembled a large plane wart. The surfaces of the lesions were smooth or slightly roughened from the partial detachment of small epidermic shreds. In two of the lesions, the hairs were broken off close to the surface and the follicles were surrounded at a little distance by a fine scaly collaret. The color of most of the lesions was light brown, and there was no peripheral erythematous zone about any of the efflorescenses. The lesions were quite firm to the touch and did not fold readily. The larger lesions gave the sensation of a tough leather disk inserted into the skin.

There was no hyperhidrosis. Attempts to demonstrate fungi by microscopic preparations and culture on Sabouraud's medium were unsuccessful.

Treatment.—The disorder resisted roentgen therapy (both fractional and subintensive doses), Whitfield's ointment, freezing with carbon dioxide snow and acid nitrate of mercury. The two latter measures were not used to their full escharotic capacity, as the patient refused to do anything that might result in permanent scarring. In view of the positive Wassermann reaction, neoarsphenamine was given for four doses (2.4 Gm. in all). The patient then decided to abandon treatment. I heard from him in March, 1929, and he said that the disease had disappeared without further treatment about a year before. I could not verify this statement by personal observation.

CASE 2.—*History.*—An unmarried Jewish merchant, aged 29, was seen on Nov. 5, 1925. With the exception of an appendectomy in 1917, he had never been seriously sick. He said that he had not had venereal disease. No member of his family had any disturbance of the skin similar to his own.

A physical examination revealed no apparent visceral abnormality. Routine blood count and urinalyses gave normal results. The Wassermann reaction was negative. Both scale preparations and dextrose agar cultures were negative for fungi in the lesions.

The skin disease for which he consulted me began in 1921. At that time he resided in Portland, Ore., and some time after its onset he consulted a dermatologist who treated him without success. The lesions were confined to the back of the hands and never gave rise to any subjective sensations, with the exception of a feeling of roughness when the hands were rubbed together. The lesions slowly enlarged to a certain size, and then remained unchanged. A new lesion occasionally appeared, but for a number of months no new ones had developed. The right hand was affected first. He had no hyperhidrosis and had never had any other disease of the skin except a bilateral tinea cruris in which fungi were demonstrable. This disease first appeared during the preceding summer several years after the lesions on the hands developed. There were five lesions on the back of the right hand and one on that of the left. The smallest was 4 mm. in diameter and nearly square. The largest lesion, roughly circular, was 3.5 cm. in its longest diameter. The position of the lesions is shown in figure 2. Their surfaces were either smooth or slightly roughened, and scratching raised a small, white, dry shred which separated with some difficulty. They were yellowish or gray with some areas showing faint redness. The hairs in the lesions had been broken off just above their exit from the follicular opening. The lesions were practically level with the surrounding surface or raised a fraction of a millimeter above it. As in the preceding case, the lesions had the firmness of tough rubber and were not readily folded though movable with the skin.

Treatment.—The lesions proved resistant to salicylic acid ointment up to 10 per cent strength, to trichloracetic acid and to Asiatic pill combined with a compound tar ointment. One lesion was removed by endothermy, but the patient refused to continue with this therapy. The patient moved to another city, and I lost track of him. While under my treatment, this patient was seen by Dr. O. S. Ormsby of Chicago, who wrote me that he had seen a number of similar cases and had classed them with the keratodermas. He had never had the opportunity of studying a lesion histologically, and when I sent him a section from case 1 he wrote that it was difficult to differentiate it from plane warts. It was Dr. Ormsby who suggested the Asiatic pill, mentioning that he had had success with it in a number of cases in which it was pushed to the limit of tolerance.

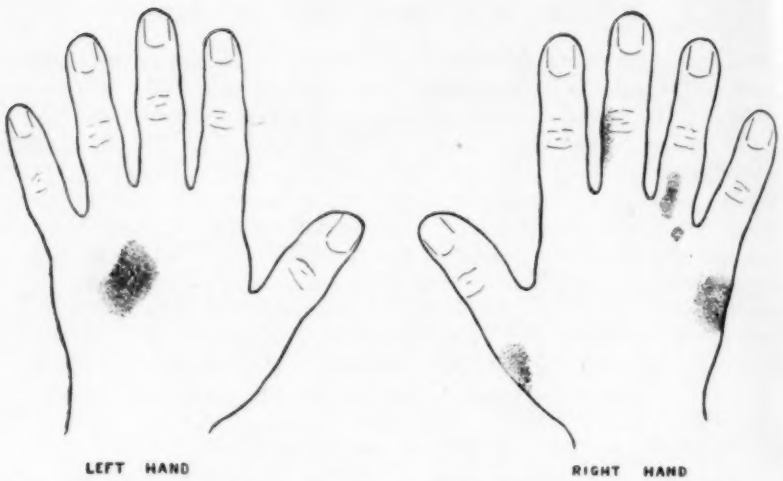

Fig. 2.—The location, relative size and shape of the lesions in case 2.

Fig. 3 (case 2).—The lesions in the patient. The photograph was taken in September, 1929, after the article had been completed. It shows changes that were not described in the text: extension of the two large lesions on the back of the hands and depigmentation where part of the lesion has involuted. On the depigmented areas are several brown spots.

CASE 3.—*History.*—McT., a married man, aged 30, an editorial writer, had never been seriously sick, and his general health and functions had been normal for many years. No member of his family had a similar skin disease. He said that he had not had venereal disease.

No visceral abnormalities were detected. A Wassermann test of the blood gave a negative result. The basal metabolic rate was —6. Neurologic examination revealed nothing of moment. There was a slight decrease of epicritic sensation in the skin lesions. Many attempts to demonstrate fungi in the lesions, both microscopically and culturally, were fruitless. On two occasions, the epidermis was completely shaved off the lesion, and the entire material thus obtained was subjected to cultural (dextrose agar) and microscopic study.

He was first seen on Nov. 1, 1927, with hyperhidrosis of the hands. This was relieved with solution of aluminum chloride. He returned in May, 1928, with the present trouble, which appeared in December, 1927. The first lesion developed on the left thumb, and from time to time other lesions appeared, usually one at

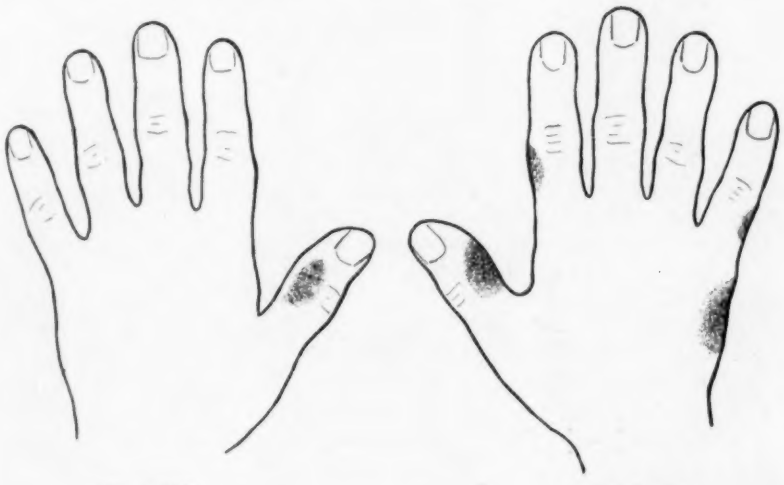

Fig. 4.—The location, relative size and shape of the lesions in case 3. It should be noted that in cases 1, 2 and 3 the lesions are not situated especially over bony prominences or at points of trauma.

a time. They caused no discomfort, except when the lesions on the fingers developed superficial fissures. They had not changed with the seasons.

Skin Disorder.—Five lesions were present; four on the right hand, and one on the left. The eruption was confined to the dorsum or lateral surfaces. Figure 4 shows their location and relative size. The lesions had been partly picked off and presented a slightly roughened surface with partial detachment of the epidermis. They varied from dull red to yellow. The lesions on the fingers, which had been picked almost clean of their corneous layer, exhibited little infiltration, while the single large lesion still retained its rubbery consistency.

This patient was under observation until April, 1929, and during that time developed two new lesions. The patient said that they first appeared as small, firm points which gradually enlarged. When seen by me about a month later, they were slightly raised, circular, flattened, yellowish disks with a smooth shiny surface.

Treatment.—Treatment in this case consisted in the application of 50 per cent solution of potassium hydroxide and silver nitrate, administration of Asiatic pills internally and later application of a mild keratolytic salve, but the condition was resistant to these measures.

HISTOLOGY

Material was obtained for histologic study from the patients in cases 1 and 3. The lesion studied in case 1 was an early one, about 4 mm. in diameter. Part of an older, large lesion was examined from case 3.

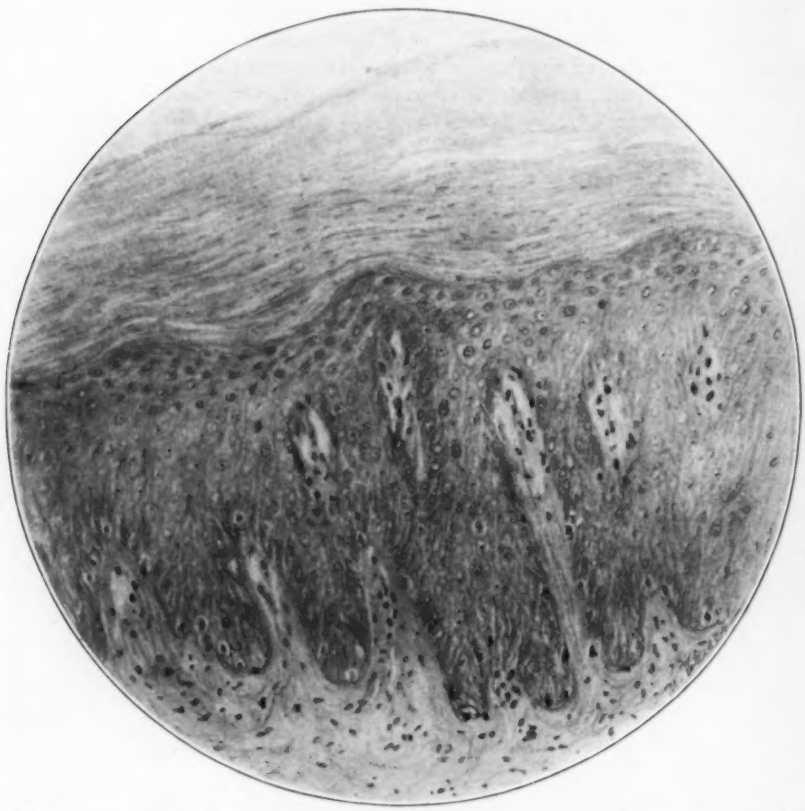

Fig. 5 (case 1).—Parakeratosis, acanthosis and moderate degree of catarrhal inflammation in the upper cutis.

The sections were embedded in paraffin and stained with hematoxylin-eosin and Weigert's elastic tissue stain. They were removed under local anesthesia.

In case 1, the most striking feature was the epidermal hypertrophy. At the edge of the lesion the corneous layer increased abruptly to about four times its normal width for this region. The larger part of this layer exhibited hyperkeratosis but there were two areas in which parakeratosis was present (fig. 5). One of these parakeratotic areas

corresponded to about three papillae; the other was much larger. The stratum lucidum was just discernible. The stratum granulosum was decidedly thickened, containing from five to twelve cells. The granules stained well except under the parakeratotic areas where the granules were hardly discernible. The rete showed marked acanthosis, chiefly in its interpapillary portion. The pegs were thin and long, somewhat

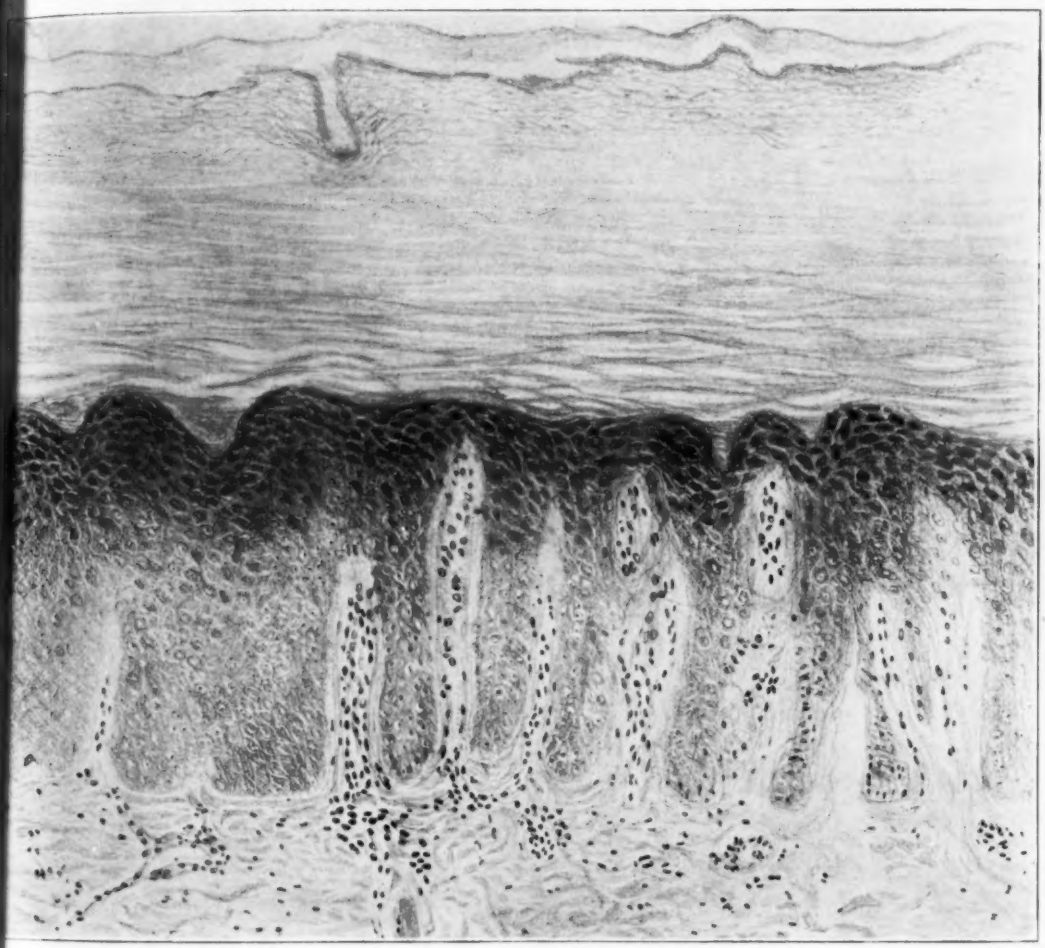

Fig. 6 (case 2).—Pure hyperkeratosis, hypergranulosis, acanthosis and an insignificant catarrhal inflammation of the papillary body.

club-shaped, but in many areas confluence had taken place with obliteration of the papillae. The cells of the rete were apparently normal. In some areas there was a moderate spongiosis without rupture of the prickle cells. There were no wandering cells in this layer. The basal layer was intact throughout. An occasional cell in this area showed perinuclear hydropic degeneration. The evidence of epidermal edema

(spongiosis, alteration cavitare) was most pronounced in the areas corresponding to the parakeratosis and to the inflammation in the upper cutis. This inflammation was moderate in intensity, consisting of slight edema of the papillae with dilatation of the blood vessels and small perivascular collections of lymphocytes and fibroblasts. This banal inflammation involved only the papillary body and immediately subjacent parts. The hair follicles were normal. Some of the coil gland

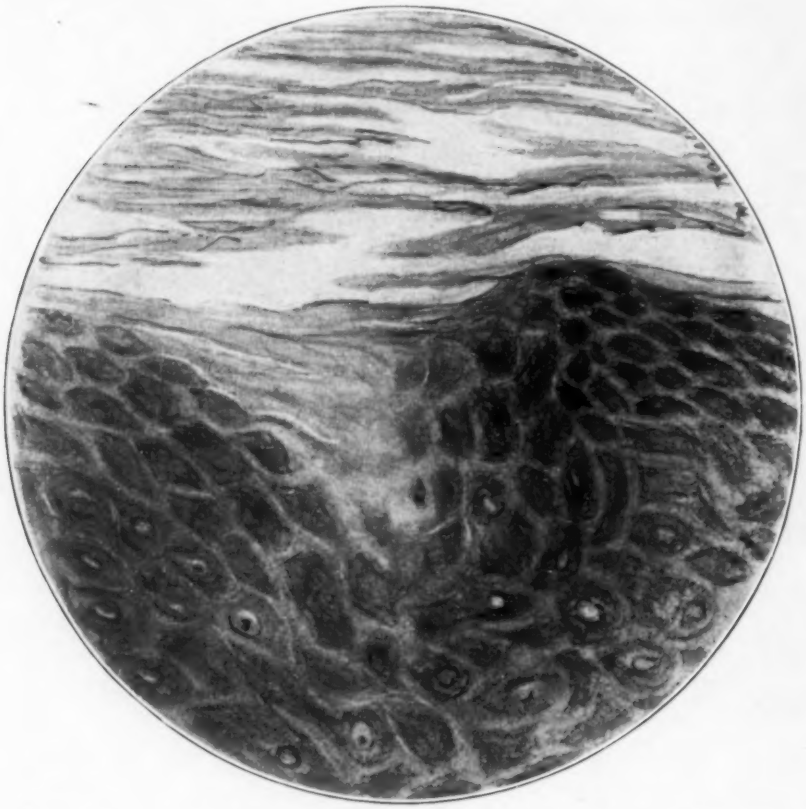

Fig. 7 (case 2).—Cleavages in the inner layers of the stratum corneum; the pure hyperkeratosis and hypergranulosis are shown.

outlets were partially blocked by a horny plug and the lumina of the glands seemed to be somewhat dilated, but there were no reactive phenomena about the glands. Neither the coil ducts nor the follicular openings exhibited any special relation to the areas of parakeratosis.

In case 3, to avoid repitition, only deviations from the previous specimen will be detailed. In this case there was a pure hyperkeratosis (fig. 6). In the stratum corneum there was a good deal of cleavage between the cells in the inner half of the layer (fig. 7). The granular

layer stained well throughout and varied from four to nine cells in width. There was practically no spongiosis and even fewer cells than in case 1, showing hydropic degeneration (fig. 8).

In the cutis, the inflammatory reaction was less than in the first case but of the same type. The dermal appendages showed no change from the normal.

In both specimens the elastic tissue appeared normal.

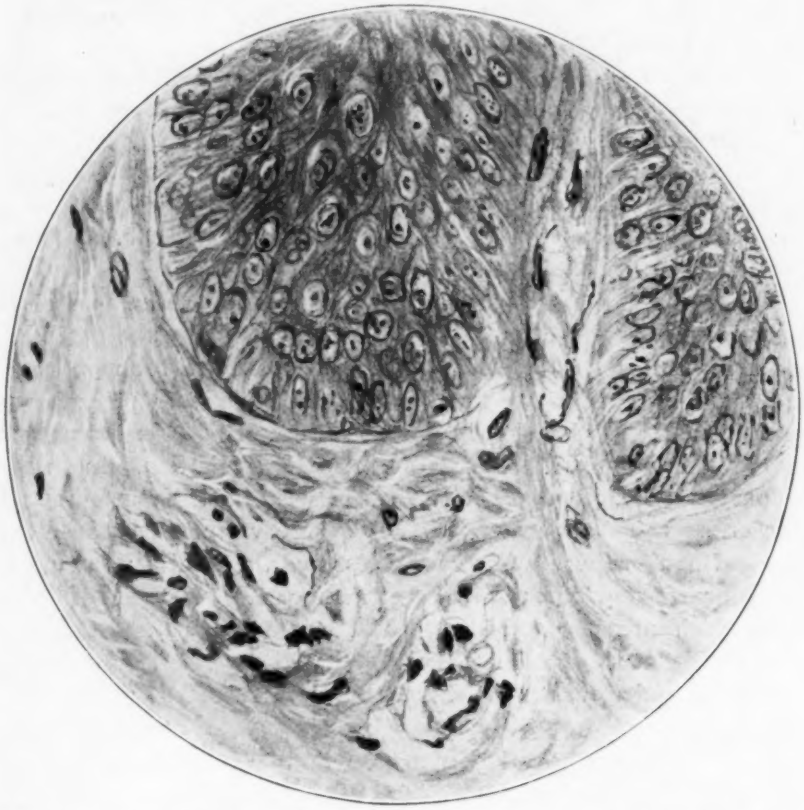

Fig. 8 (case 2).—The regular acanthosis, the sharp epidermal papillary demarcation and the character of the inflammation in the upper cutis.

The histologic changes, therefore, were: (1) predominant hyperkeratosis, occasional parakeratosis, (2) hypergranulosis, (3) acanthosis and (4) an insignificant inflammation of a banal type in the upper cutis.

DIFFERENTIAL DIAGNOSIS

From the foregoing histories and pathologic study, it will be seen that no difficulty is encountered in differentiating these cases from the rare keratodermic entities appearing in these regions, such as, angio-

keratoma, keratoderma blennorrhagica, porakeratosis and helioderma simplex et annularis.

The literature of the past ten years contains a few isolated reports of discrete keratodermic lesions on the back of the hands, such as, Krupnikoff's [1] case in which pityriasis lichenoides chronica was present, Hidaka's [2] keratoangioma punctatum symmetricum and Chevallier and Flandrin's [3] keratodermite en ilots des mains et des pieds chez un adult, but none of these resembles the cases under discussion. From statements of the patients and my own observation, occupational, traumatic and toxic (arsenic, etc.) causes can be eliminated.

The greater difficulty appears in a differentiation from some of the common disorders of the skin. Symptomatic keratodermas are well known in a number of cutaneous maladies, and secondary hyperkeratotic transformation is a common clinical observation. It seems likely that many observers have been satisfied to classify these cases as manifestations, perhaps somewhat unusual, of such common dermatoses as psoriasis, dermatophytosis, etc.

The essential features of my cases, besides the appearance of the lesions, were the limitation to the backs of the hands, the absence of subjective sensations, the slow course without change for months at a time and the obstinacy to therapy. Moreover, all my patients were young men in good health. In one patient latent syphilis was present, but the lesions were uninfluenced by syphilitic medication. In another, the onset was preceded by hyperhidrosis, while in the remaining case, tinea cruris was found; the latter was evidently an adventitious occurrence. But there was no associated psoriasis, pityriasis rubra pilaris, eczema or lichen planus, and so far as these or other generalized dermatoses which might conceivably produce such lesions are concerned, it hardly seems reasonable to believe that three cases, so similar in appearance and manifestations, would have occurred as prodromal or abortive manifestations of one of these common disorders.

I have seen patches of psoriasis on the dorsa of the hands associated with the usual generalized manifestations of that disease. In these patches the scale was looser, there was a more pronounced hyperemia and the histology was different. Histologically, psoriasis on the back of the hands differs grossly from the present cases by showing less marked hypertrophy of the horny layer and a more intense inflammatory reaction in the upper cutis. Psoriatic lesions, even in this location, are not particularly resistant to treatment.

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2. Hidaka: Abstr., Zentralbl. f. Haut. u. Geschltkrankh. **18**:371, 1926.

3. Chevallier, P., and Flandrin, P.: Bull. Soc. franç. de dermat. et syph. **34**:743, 1927.

Eczema may produce hyperkeratotic patches on the hands, associated, however, with other forms of the disease elsewhere, or if confined to the hands preceded or accompanied by other types of the disease. It is usually accompanied by subjective symptoms and characterized histologically by vesicle formation.

Keratoderma palmaris et plantaris need be mentioned only because some cases of this disease exhibit lesions on the back of the hands, but, of course, only in association with the disease in its normal location. The disease is usually diffuse though discrete and striate forms are well known. The attempt of Brauer and Buschke and Fischer to erect independent entities of the latter varieties has not been generally accepted.

In respect to my own cases, a report of a case by Rinsema [4] should be mentioned. Rinsema's patient was a man, aged 30, who presented numerous horny papules predominantly on the back of the hands. The sister of this patient exhibited a characteristic example of keratodermia maculosa disseminata symmetrica palmaris et plantaris (Buschke-Fischer) which, as already mentioned, is probably a subvariety of keratoderma palmaris et plantaris. The location of the disorder in Rinsema's male patient alone brings it into consideration with my cases; the familial occurrence and other features which need not be detailed here sufficiently distinguish it.

Verruca plana shows many histologic similarities with my cases. Clinically, the resemblance between the two conditions is not close, even the unusual cases of giant plane warts presenting features that differentiate them. These features are the angularity, the more superficial position, lack of scaling and softer consistency of plane warts. I must say, however, that giant verruca plana was the original diagnosis in the first case until study convinced me that it could not be maintained.

The careful and thorough but fruitless attempts to discover fungi in these cases seem to rule out a diagnosis of dermatophytosis, though it is conceivable that that diagnosis might be entertained. The hyperkeratotic (callus) forms of dermatophytosis are common enough; in my experience they appear most frequently on the soles and are rare as a discrete callus-like form on the back of the hands. The hyperkeratotic type of this disease is often a secondary change, beginning in the common vesicular or superficial squamous types.

COMMENT

From the foregoing it seems that serious consideration should be given these cases as representatives of an hitherto unrecognized clinical entity. At the same time, it must be admitted that nothing definite has

4. Rinsema, P. G.: Acta derm.-venereol. **6**:299, 1924.

been determined in regard to its causation. Etiologic investigation of the cases, admittedly incomplete, gave no clue to their nature. However, certain speculations along this line of thought may be permitted.

That it is an acquired disturbance is evident, but three cases by themselves do not allow any broad deductions as to the predisposing factor or factors. The three patients were young men; whether it occurs only in young males remains to be seen from further experience. An occupational cause could be definitely ruled out in these cases. This applies as well, it would appear from the statements of the patients, to toxic causes, such as, drugs and systemic disorders. The fact that the condition was associated with different diseases (syphilis, hyperhidrosis, tinea cruris) in each case makes it improbable that any one of them was of great moment as a direct or predisposing factor. The reasons why it does not seem to be a manifestation of one of the rare or common disorders of the skin have already been given. It is not a familial disorder. In one patient, special neurologic examination showed no indication that it was of neurotrophic origin. In each of the patients examination for fungi was negative. None of the culture tubes (dextrose agar and Sabouraud's mediums) showed any growth of bacteria. Bacteriologic examinations were not followed further.

Despite these negative observations, it seems to me that the most logical presumption is that the condition is of parasitic origin. The reasons for this assumption are that it is an acquired disease, limited in distribution and unassociated with any systemic phenomena. It is regretted that auto-inoculation and hetero-inoculation experiments could not be performed, but these patients were private ones and would not permit extensive investigation.

The histologic structure of the two cases varied in degree rather than in kind. The lesion studied in case 1 was smaller and more recent than that from case 2. In the former case a greater inflammatory reaction was found in the cutis, which had secondarily involved the epidermis to such an extent as to produce an abnormal change in the process of keratinization. That the dermal disturbance was primary and the changes in the epidermis consequent on it, is shown by the fact that the parakeratotic areas overlay those areas of the derma which exhibited the most pronounced inflammatory features. In case 2 the dermal inflammation had never reached the intensity of case 1 or had abated, so that the epidermis was not affected to the extent of interference with normal keratinization; in this instance, the process was merely quickened; producing hypertrophy. The histology, however, showed fairly clearly how the clinical picture had been produced. The rubbery consistency was occasioned by retial and horny layer hypertrophy. There seemed to be a tendency for the newly formed horny cells to separate normally as revealed by the fissures and cleavages in

the innermost layers of the stratum corneum, particularly shown in case 2. But normal desquamation did not occur and in the outer layers of the horny layer the cells had become welded together, producing the dense callus-like surface.

The nuances of color were due to varying degrees of vascular participation and to adventitious circumstances; dirt, secretions, etc.

Finally, it is apparent that these cases, if they are accepted as an entity, must be classed among the acquired keratodermas.

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ABSTRACT OF DISCUSSION

DR. MACKEE, New York: I believe that Dr. Michael is correct in labeling the condition that he has described an entity, rather than in classifying it with some other disease. I cannot classify it, but clinically the individual lesions resemble to some extent a very large, flat wart, larger than any that I have ever seen. The pathology seems to be too active for warts but not active enough for psoriasis.

I can add but little except in repetition, as Dr. Michael has described the condition thoroughly. He mentioned the stubbornness of the disease, and the fact that the lesions are difficult to see but can be felt, and so forth. The classification, diagnosis and treatment of these lesions have bothered me in the past, and the reason is that I have happened to see them associated with other disorders. A few patients with such lesions have had psoriasis, and I thought that they were aberrant lesions of psoriasis. In other cases, they have been associated with hyperkeratosis, and I thought that they were lesions of that disorder. Later I saw patients with these lesions and no other lesions, and I did not know how to classify them. I have treated the patients with the roentgen ray, and my recollection is that in one or two instances the lesions disappeared promptly, only to return within a short time. In addition to looking like large flat warts, they also look like callous spots. They usually occur in men, as a rule in younger men, and on the face and fingers. I have had golf players consult me about these lesions and try to prove to me that they hold their golf clubs in such position that they press on the areas involved, but the lesions persisted through the winter, and in one case in which the patient did not play golf for two years, which made me feel that we were not dealing with truly callous lesions.

Dr. Michael deserves credit for recognizing and calling attention to a dermatosis that has escaped the attention of all but a few dermatologists.

DR. WISE, New York: I believe that in spite of the apparent commonplaceness of these lesions, Dr. Michael has described a condition which has heretofore not been published. Pointing to the rarity of the condition, I have seen but one case; I think that a brief description of that case is justifiable. It occurred in a lawyer, aged 45, who did not play golf and who used no tools that were likely to come in contact with the area involved, which is the left side of the hand. The lesion was about the size of a dollar, but ovoid, and was of five years' duration when first seen four years ago. During that time, I have attempted by all the means I know, except surgical resection, to eradicate the lesion, but without success. The patient faithfully visited my office at regular intervals. During the first fifteen months, he paid his fees, but after that I told him voluntarily that I would treat him for nothing. He has received roentgenotherapy and carbon dioxide snow. When these were unsuccessful I used the electrodesiccating cur-

rent; that relieved the condition for only a few weeks. The lesion then reappeared exactly as it was before. The reason I realized that I was dealing with the disease described by Dr. Michael is because of the almost incredible obstinacy toward treatment, and it is this, in the absence of other lesions on the body, which characterized the lesions. I am sure that we are dealing with some hitherto undescribed lesion not in the nature of callus, not due to the use of tools or golf clubs and not associated with a dermatophytosis that is apt to lead to a persistent hyperkeratosis, especially of the plantar surface.

DR. FINNERUD, Chicago: I saw one of the cases described by Dr. Michael and possibly one other, and I can subscribe in both instances to the histologic observations and, I believe, to everything he said. Clinically, I thought that these were both possibly some form of keratoderma, although unassociated with lesions elsewhere, just as we sometimes see keratoderma affecting largely the dorsal surfaces of the joints, particularly those of the fingers.

DR. CANNON, New York: I have seen a number of these cases and am of the impression that the condition occurs not infrequently. I remember one man, a house painter, who had four times the normal content of arsenic in his blood and urine. Subsequently, I treated four other patients, each one showing an excess of arsenic in his blood and urine. I considered the disease a hyperkeratosis belonging to the neurodermite group and probably due to a variety of causes, arsenic being one of them. The most satisfactory treatment was the administration of sodium thiosulphate and desiccation, followed by the application of Unna's gelatin glue.

DR. MICHAEL, Houston, Texas: I, too, believe that these cases are not particularly uncommon, and think that they have escaped recognition because dermatologists have felt that they might be classified among the well known conditions of the skin. I think that they are not readily classified, and that they may possibly be an entity. I was interested in what Dr. Cannon said, for I obtained no clue as to the etiologic factor, and along with Dr. MacKee and Dr. Wise found no treatment of value.

DERMATITIS NODULARIS NECROTICA

REPORT OF A CASE AND REVIEW OF THE LITERATURE *

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In 1910, Werther [1] first described and reported an unusual cutaneous manifestation (fig. 1) to which he gave the name "dermatitis nodularis necrotica." Since that time, there have appeared reports of only four other cases presenting an identical clinical picture. During the past three years, such a case has been under observation at the University Hospital, and therefore it was deemed advisable to add a detailed description of this case to the existing literature.

Werther's [1] case had been under his observation for eleven years. The patient, a man, presented a chronic and recurrent eruption which was symmetrically placed, and was most marked about the dorsa of the hands and feet, the knees and elbows, the penis and the ears. The eruption consisted of bluish-black papules, averaging in size that of a cherry pit, bluish-red plaques, vesicles filled with blood or blood and pus and ulcers as large as a quarter (25 mm.). Remains of previous lesions were also present in the form of atrophic and hypertrophic scars, some being surrounded by a pigmented border, and associated with a scale. Tubercle bacilli were demonstrated in the sputum of this patient, the tuberculin reaction was positive, and moist râles could be heard over the apex of the right lung.

Histologic examination revealed a marked inflammation of the vessels down through the subcutis. In the region of the sweat glands, there was arteritis and periarteritis even to total obliteration. Phlebitis and periphlebitis were also present. In part, the tubules of the sweat glands exhibited parenchymatous degeneration; they were separated by edema, and here and there in the coil glands there were massive leukocytic infiltrates, and beginning abscess formation. Throughout the cutis, there was exudation and hemorrhage, and the connective tissue bundles were torn apart. The lower borders of the rete were disturbed by an

* Submitted for publication, July 30, 1929.

* Studies and contributions of the Department of Dermatology and Syphilology of the University of Michigan Medical School; service of Dr. Udo J. Wile.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 10, 1929.

1. Werther: Dermatitis Nodularis Necrotica, Ikonographia, 1910, p. 213.

exudate, and here one saw intra-epithelial pustules and subepithelial abscesses made up of leukocytes and red blood cells. Tuberculous granulation tissue and organisms were not found. The inflammatory infiltrate consisted of leukocytes, lymphocytes and plasma cells, Eosinophils were also found in great numbers, and often grouped together.

From these observations Werther [1] concluded that the process was primarily an endarteritis with acute inflammatory changes in the cutis, accompanied by hemorrhage, abscess formation and necrosis in and

Fig. 1.—Dermatitis nodularis necrotica, Werther's case. Taken from the Ikonographia.

about the sweat glands. This picture was compatible in his mind with the pemphigoid and pseudofuruncular eruptions, but the clinical residual was that of a papulonecrotic tuberculid, and his explanation was that of a hemorrhagic infarct with embolic plugging of the end arteries. Under arsenic in the form of injections and Asiatic pills, and general treatment for tuberculosis, the patient became entirely well and remained well.

Werther [1] concluded that the skin manifestations must be classed among the tuberculids on account of the coincident pulmonary tuber-

culosis, the symmetry of the eruption, its predilection for the extremities, its chronic course, its response to arsenic, and the histologic observation of endarteritis which is found in all tuberculids.

In the following year, Klingmüller [2] reported the case of a girl, aged 20, presenting a polymorphous eruption which had been present from her tenth to her eighteenth year. It came in recurrent attacks, and occupied the extensor surfaces of the extremities, especially about the knees, elbows and hands, but which also involved the remainder of the body except the head and face. The lesions were of three types: First, bluish-red papules appeared surrounded by an inflammatory zone, on the summit of which there rapidly developed a pustule which quickly became covered with a dried down crust. In place of this evolution, there would be a bloody extravasation which persisted for days or weeks as a stippled hemorrhage, and finally involuted with pigmentation. The papules became confluent to form larger plaques, the central portion of which became hemorrhagic. These involuted, or ulcerated, forming ulcers with a necrotic base, irregular border and firm or soft zone of infiltration about them. These infiltrates and ulcers healed slowly, leaving round or serpiginous scars with peripheral brownish hyperpigmentation, which eventually also faded.

In addition, plaquelike infiltrates arose without the previous papulopustular stage. Their involution was not different from those previously mentioned. Lastly, there were smaller and larger bluish-red and red macules, which passed over quickly or became the basis of the other two types of lesions.

At times, the eruption was accompanied by a slight rise in temperature, and the patient complained of exhaustion and malaise. The ulcerations were painful.

The composite histologic picture was that of a perivascular infiltration, particularly in the subpapillary layer of polymorphonuclear leukocytes; infiltration and miliary abscesses of the epidermis, and hemorrhages into the cutis and papillae. Cultures of the lesions and of the blood remained sterile, and tubercle bacilli were not found.

Frohwein, who examined the histologic material, regarded the picture as that of angiokeratoma, but Klingmüller [2] maintained that he erred because he did not look on the abscesses as being of an inflammatory nature, and did not attach sufficient weight to the inflammatory changes. Kingmüller [2] pointed out further, that the condition need not necessarily be of tuberculous etiology, since in his case the favorable influence of arsenic was not noted; there was an absence of a local or general reaction to tuberculin; the histologic changes were

2. Klingmüller: Ueber Dermatitis Nodularis Necrotica, Arch. f. Dermat. u. Syph. **110**:419, 1911.

not specific, and spontaneous healing occurred after ten years. He pointed out also that the symmetry of the eruption, and its predilection for the extremities is also found in erythema multiforme, as well as in lupus pernio, and the papulonecrotic tuberculids. The chronic character of the eruption furthermore, is not real because the exacerbations have a distinctly acute character. He agreed with Werther [1] in calling the condition dermatitis nodularis necrotica, but regarded it as a purely inflammatory dermatosis of hematogenous origin.

Clinically, Werther's [1] and Klingmüller's [2] cases are indentical, differing only in that in the former there was a tuberculous etiology whereas in the latter there was not.

Cases of clinical similarity were reported by Urban,[3] Bruck,[4] Balzer and Alquier,[5] Leredde and Haury,[6] Leredde and Milian,[7] Du Castel,[8] Hallopeau,[9] Hallopeau and Norero,[10] Lutz,[11] Thibierge,[12] Gaucher,[13] Hallopeau and Damany,[14] Delbanco,[15] Philippson,[16] Boeck,[17] Grune-

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3. Urban: Dermatitis Nodularis Necroticans tuberculosa, Ikonographia, 1910, p. 209.

4. Bruck: Dermatitis Nodularis Necrotica, suppurativa et ulcerosa, Ikonographia, 1912, p. 231.

5. Balzer and Alquier: Tuberculide multiforme très étendue, Ann. de dermat. et syph. **1**:1171, 1900; ibid. **2**:47, 1901.

6. Leredde and Haury: Tuberculides angiomateuses et hypertrophiques multiples coincident avec des lésions tuberculeuses des poumons et des ganglions, Ann. de dermat. et syph. **10**:384, 1899.

7. Leredde and Milian: Tuberculide angiomateuse des membres inférieurs, Ann. de dermat. et syph. **9**:1095, 1898.

8. Du Castel: Eruption purpurique des doigts, Ann. de dermat. et syph. **7**:724, 1896; Dermatite hémorrhagique des saillies articulaires des doigts, ibid. **10**:141, 1899; Tuberculides des membres, ibid. **2**:959, 1901.

9. Hallopeau: Sur une forme bulleuse de toxi-tuberculides, Ann. de dermat. et syph. **4**:35, 1903.

10. Hallopeau and Norero: Sur une forme vésiculo-pustuleuse de toxituberculides, Ann. de dermat. et syph. **5**:556, 1904.

11. Lutz: Ueber eine bisher nicht beschriebene Dermatose: Haemorrhagisches, papulo-bullöses und ulzeröses Exanthem, verursacht durch hämatogene Infektion mit gramnegativen Bazillen, Arch. f. Dermat. u. Syph. **121**:613, 1915. On further study this case proved to be one of glanders.

12. Thibierge: Foliculites disséminées prédominant aux mains et aux oréilles chez un sujet atteint de polyadénopathies tuberculeuses, Ann. de dermat. et syph. **8**:50, 1897.

13. Gaucher: Tuberkulose pustulo-ulcéreuse: Maladies de la peau, 1909, p. 379.

14. Hallopeau and le Damany: Lupus érythémateux anormal, folliclis, ou type morbide nouveau? Ann. de dermat. et syph. **6**:380, 1895.

15. Delbanco: Ein Fall von Lupus erythematosus disseminatus Boeck, Monatschr. f. prakt. Dermat. **31**:176, 1900.

16. Philippson: Phlebitis nodularis necrotisans, Arch. f. Dermat. u. Syph. **55**: 215, 1901.

17. Boeck: Lupus erythematosus disseminatus Boeck, Arch. f. Dermat. u. Syph. **42**:71, 1898.

wald,[18] Spiegel,[19] Török,[20] Stillians and Oliver,[21] Fink,[22] Haxthausen,[23] Rille,[24] Balzer and Milian,[25] and most recently Milian.[26] In the majority of these cases, there was evidence of tuberculosis, either histologically in the skin lesions themselves, or otherwise clinically in the patients. In nine cases, there was no evidence whatever of tuberculosis, and it is these cases that compare more favorably to the one reported by Klingmüller,[2] while the others compare more favorably to the one originally described by Werther.[1]

In Urban's [3] case, the lesions were papular in type, tended to remain discrete, and showed some central necrosis. Histologic examination revealed tuberculous architecture in the central portion of the lesion, without caseation. The patient died after seven weeks of observation, and the autopsy observations were that of a tuberculous meningitis and early miliary tuberculosis.

Bruck,[4] in 1912, reported two cases presenting similar eruptions (fig. 2), involving both legs, the knees and buttocks. The lesions were of the papulonecrotic type, and in one case on several occasions, vesicles were seen which soon became pustular. Both patients showed a general reaction to tuberculin; they were specifically influenced by tuberculin therapy; they had a chronic recurrent tendency, and the appearance, localization and evolution of the lesions was similar to that of a papulonecrotic tuberculid. According to Jadassohn, who examined the histologic material, the picture was that of a tuberculosis standing between the two Darier types; the nonspecific vascular form, and the form presenting a purely tuberculous architecture. These two cases are similar to that reported by Werther,[1] except for the hemorrhage.

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18. Grunewald: Acne varioliformis universalis, Monatschr. f. prakt. Dermat. **4**:81, 1885.

19. Spiegel: Folliculitis generalisata, Monatschr. f. prakt. Dermat. **23**:617, 1896.

20. Török: Dermatitis Nodularis Necrotica, Arch. f. Dermat. u. Syph. **58**: 339, 1901.

21. Stillians and Oliver: Dermatitis Nodularis Necrotica: Report of Case, Arch. Derm. & Syph. **3**:843 (June) 1921.

22. Fink, H. W.: Dermatitis Nodularis (Necrotica): Report of Case, Arch. Dermat. & Syph. **7**:704 (May) 1923.

23. Haxthausen: Dermatitis Nodularis Necrotica (Werther), Verhandl. der. Dän. dermatol. Ges., 1923-1924, p. 28.

24. Rille: Dermatitis nodularis necrotica, suppurative et ulcerose, Ber. d. Mitteldtsch. Dermatol. Gesellsh., Leipzig **20**:3, 1921; abstr., Zentralbl. f. Haut- u-Beschlectskr. **1**:419, 1921.

25. Balzer and Milian: Tuberculose cutanée pustulo-ulcéreuse, Soc. française de dermat. et syph. **21**:79, 1910.

26. Milian: Tuberculides bulleuses purpuriques ulcéreuses, Paris méd. **67**:75, 1928.

Lutz,[11] in 1916, reported what he thought to be a previously undescribed dermatosis, in a woman, aged 44. The eruption (figs. 3 and 4) had been present for three years, was distinctly polymorphous in character, and involved particularly the back and buttocks, the hands, legs and feet. Clinically and histologically, this case (fig. 5) was identical with the one reported here and the one previously described by Klingmüller.[2] The Wassermann and tuberculin reactions were

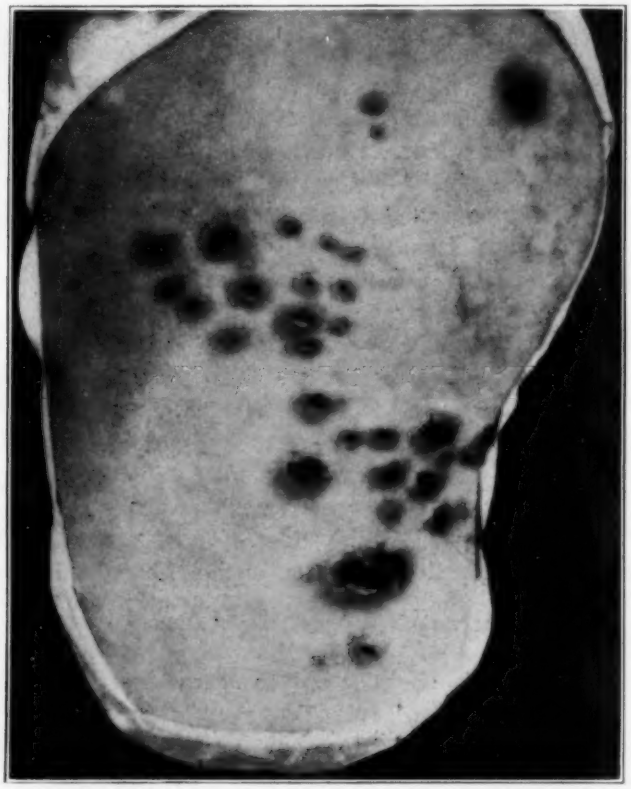

Fig. 2.—Dermatitis nodularis necrotica, Bruck's case. Taken from the Ikonographia.

negative, and after a trial of various types of treatment, the condition responded to neoarsphenamine. On one occasion, a gram-negative bacillus was cultured from the blood stream on neutral agar. The author thought this organism was the etiologic factor in the production of the eruption. He was, however, unable to repeat the positive blood culture or to make a subculture of the organism.

Other cases previously reported and resembling both Werther's [1] and Klingmüller's [2] are those by Balzer and Alquier [5] in which the lesions were bluish-red, almost hemorrhagic papules, particularly on

the extensor surfaces. There were also many large bluish-red plaques with definite infiltration and central crusting. Atrophic red and white shiny scars remained from previous lesions. Histologically, the epidermis was normal, with perivascular infiltration, and many hemorrhages in the papillary layer. There was no evidence of tuberculosis in the patient, and healing took place gradually under treatment with collodion of sulphonated bitumen after two and one-half years.

Fig. 3.—Lutz' case (general view). Taken from Arch. f. Dermat. u. Syph.

Leredde and Haury [6] reported the case of a boy, aged 15 years, in whom the eruption involved the forearms and hands, and was ushered in with painful swelling of the hands and feet. The exanthem was of two types, small deep red or bluish-red, pea-sized infiltrates, and long or round infiltrated plaques, some hyperkeratotic, others with hemorrhagic pinpoint lesions in them. The histologic picture was that of angiokeratoma, and showed perivascular infiltration of lymphocytes, polynuclears and eosinophils. There were no plasma, giant or epithelioid

cells. The patient showed tuberculous involvement of both apexes, with multiple lymphadenitis and softening of the inguinal glands.

In Leredde and Milian's [7] case the eruption was similar to that just described, and the neck glands were of the size of a hen's egg. The histologic examination was also comparable to that in Leredde and Haury's case, with the additional observations of thrombophlebitis, and endarteritis obliterans.

Fig. 4.—Lutz' case (close-up). Taken from Arch. f. Dermat. u. Syph.

Du Castel [8] made observations on several occasions in a man, aged 33, who in his youth, had an eruption on the lower extremities which left many round superficial white scars. At the same time a papular eruption appeared on the legs, which ulcerated and involuted with scarring. Recurrences were accompanied by fever, loss of appetite and insomnia. Some of the papules showed a depressed center, which was pale red, and partly hemorrhagic. The ulcers were surrounded by a peripheral zone of infiltration. Some of the lesions involuted, leaving pigment, others became hemorrhagic in the central portion, and healing took place slowly with residual pigment or purpura.

Hallopeau,[9] recorded the case of a man, aged 32, who for eight years had an eruption involving the legs, thighs, lateral and posterior surfaces of the hips, and the arms and hands only sparsely. Both papular and vesicular lesions were present with crusting, and finally scar formation.

Together with Norero,[10] Hallopeau reported another case, which they termed a "vesicopustular toxituberculid." In this patient, the eruption was present for seven years. The submaxillary glands were greatly enlarged and softened, and there were scars in the neck. The right pulmonary apex showed evidences of tuberculosis. The lesions were papulonecrotic in type, and occurred in great numbers on the extremities, especially the knees, feet and elbows. Together with this,

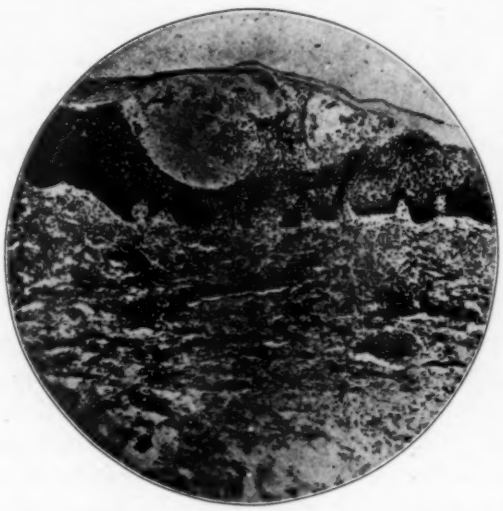

Fig. 5.—Photomicrograph from Lutz' case. Compare with figure 13. Taken from Arch. f. Dermat. u. Syph.

vesicopustular lesions were also present with or without an inflammatory halo. On the lower extremities, there were also infiltrated plaques as large as 5 cm. in diameter. Healing took place with scarring which at first was dark violet, then brown, and finally white.

Thibierge,[12] reported a case in which both tuberculosis and frostbite were elicited in the history. The eruption, which was of one-half year's duration, was papulopustular in type with central crusting, and healing with a round slightly depressed scar, which at first was pigmented, but later became white.

Gaucher [13] reported a case in which the clinical picture was similar to that reported by Werther [1] and Klingmüller,[2] except that the lesions never became confluent. Tubercle bacilli were readily demonstrated in the lesion in this case.

Hallopeau [27] contributed a further case in which the eruption was papulopustular in type, partially confluent and with peripheral pemphigoid lesions. When involution took place, there remained a slightly erythematous macule, or the minutest depressed scar. Some of the lesions were similar to those of lichen scrofulosorum. Another case by the same author [28] presented the picture of a disseminated and agminated suppurative folliculitis. Together with Damany,[14] a third case was reported by Hallopeau in a young woman, aged 22, who had had glands in the neck that were large, firm and painful to palpation for one year. The eruption, which involved the fingers, hands, lower arms, elbows and knees, was of six months' duration, and was distinctly polymorphous in type. There were papules, papulopustules, vesicles and ulcerations surrounded by an inflammatory zone. Healing took place with depressed scars. The histologic examination revealed a diffuse round and plasma cell infiltration of the papillary layer with perivascular infiltration of the cutis. There was also distention of the vessels and lymphatics, and small hemorrhages. A slight amount of intercellular edema was present. Their diagnosis was that of an atypical lupus erythematodes.

Delbanco [15] reported the case of a woman aged 24, who since early youth had scrofuloderma, and who five years previously was operated on for tuberculous neck glands. For the past two years, an eruption had been present on the ears, dorsa of the hands and buttocks, which began as split pea sized bluish-red papules, which gradually enlarged and developed a necrotic center. After the crust came away, there remained a deep scar, which gradually became even with the surface of the surrounding skin. A focus of tuberculosis was discovered in the tendon sheath of the extensor pollicis longis of the left hand.

Philippson,[16] reported a case that clinically conformed to those reported by Darier, Boeck, Barthelemy, Hallopeau, and others, but he pointed out that pathologically his case was not in accord with the cases of these authors. He believed the chief pathologic process to be in the deep subcutaneous tissue, which is often overlooked, and which in his case presented a phlebitis with secondary necrosis.

Cases reported by Boeck,[17] Grunewald,[18] Spiegel [19] and Török,[20] exhibit in part some of the characteristics of the cases described by Werther and Klingmüller.[2] The type of lesion was for the most part papulonecrotic and nodulo-ulcerative; the vesicular and hemorrhagic types were not encountered.

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27. Hallopeau: Sur une nouvelle forme suppurative et pemphigoïde de tuberculose cutanée en placards à progression excentrique, etc., Ann. de dermat. et syph. **6**:1093, 1895; ibid. **7**:34, 1896; ibid. **2**:167, 1901.

28. Hallopeau: Tuberculose cutanées engendrées par des toxines émanées de foyers plus ou moin éloignés, Ann. de dermat. et syph. **7**:1019, 1896.

In this country, Stillians and Oliver,[21] and later Fink,[22] presented the case of a white laborer, aged 43, who had a chronic and recurrent eruption of seven years' duration, involving the head, trunk, back and extremities. The case was first seen and the diagnosis made by the late Frederick Harris. The lesions were discrete, oval or circular, copper-colored indurated papules, which varied in size from that of a pea to that of a quarter (25 mm.), the central portion of which became necrotic, and covered with a thick black crust. No mention was made of vesicular or hemorrhagic lesions, and histologic studies were not available.

In Haxthausen's [23] case, the lesions were pustulohemorrhagic with central necrosis, but confined to the region about the ankles. The Pirquet reaction was strongly positive, and the histologic observations were similar to those in Werther's [1] case.

Rille's [24] case was probably identical with the one reported by Bruck,[4] and involved only the buttocks and upper portion of the thighs. Healing took place under the application of ointments and dressings after one-half year.

In Balzer and Milian's [25] case the lesions were of the pustulo-ulcerative type, and involved the extremities, buttocks and lumbar region. The legs and extensor surfaces of the arms were markedly involved, while the face was spared. The back showed only scarring. The eruption, which was of three years' duration, occurred in a girl, aged 9, whose general examination was negative, except for a polyadenitis. Guinea-pig inoculation was positive, and histologic examination revealed a lymphoid hyperplasia with edema, dilatation of the vessels and many small hemorrhages. Some of the sections showed giant cells. This case was presented as one of the rare types of pustulo-ulcerative tuberculids.

Most recently, Milian [20] reported a case in which the eruption involved the hands, feet and legs, and was bullous, hemorrhagic and ulcerative in type. Auto-inoculation with fluid from a bulla produced a pustule which later ulcerated. Microscopic examination of a lymph gland revealed caseation, and a tuberculous architecture. The tuberculin test produced a bulla, which passed through the same stages as the other bullous lesions. Histologic examination of biopsy material did not reveal anything diagnostic of tuberculosis.

During the past three years, a case of dermatitis nodularis necrotica has been under observation in the dermatologic clinic of the University of Michigan Hospital, and on account of the rarity of the condition, its disputed etiology and unusual clinical features, it was deemed advisable to add a detailed description of this case to the existing literature.

REPORT OF CASE

History.—R. S., a school girl, aged 8, who registered at the University Hospital, Nov. 15, 1926, and whose family and birth history was entirely negative, had measles at the age of 2, and quinsy three months before admission. The patient has always been troubled with enuresis. One year previous to admission, an eruption appeared over the upper portion of the back, scalp and ears, spreading to involve the buttocks and extremities, which was in the nature of "boils," and which

Fig. 6.—Author's case showing extent of eruption and the sites of predilection.

involuted leaving scars. At first the lesions were painful, but as they became older, the pain disappeared. These "boils" were incised and drained, but new ones appeared, so that at no time has the patient been entirely free from them, although she has had many forms of treatment. The glands of the groin at one time swelled, ruptured and discharged.

Examination.—The patient was rather undernourished, and somewhat pale, but apparently not acutely ill. The results of the physical examination were entirely negative except for the skin, which presented a generalized polymorphous eruption (fig. 6), which showed a predilection for the buttocks, the lower extremities, particu-

larly about the knees and feet (extensor surfaces), the upper extremities, particularly about the elbows (extensor surfaces), and the dorsa of both hands. The individual lesions varied in size from pinhead to that of a cherry, the younger ones were bright red, while the older ones were brownish or bluish red. Some of them were elevated rather sharply and others were flatter. For the most part the lesions were papular, vesicular, vesicopustular, hemorrhagic and ulcerative, and over the upper part of the back, where they had involuted, there were many atrophic and

Fig. 7.—Close-up of buttocks and legs, showing various types of lesions.

Fig. 8.—Close-up of knees and lower legs, showing ulcers over knees.

hypertrophic, both round and oval scars (figs. 7 and 8), varying in size from pinhead to that of a dime (18 mm.). Ulcerating lesions were present over the knees and elbows (fig. 9), and were covered with a brownish-black crust, and surrounded with a halo of bright erythema. These were distinctly tender to palpation. There was a generalized lymphadenitis, including both epitrochlears, varying in size from that of a pea to that of a large bean, and in the inguinal regions there was some irregular, puckered scarring at the site of previously broken down inguinal glands.

Six months previous to her entrance in the University Hospital, the patient came under a physician's care because of a "swelling in the neck and skin trouble of six months' duration." The swelling in the neck was a retropharyngeal abscess, and was quickly cared for. At that time, the skin condition was essentially the same as when I first saw the patient.

The tuberculin and Wassermann reactions were negative. The urine showed gross blood, casts, leukocytes and albumin. Hemoglobin was 44 per cent; the red blood cells numbered 3,200,000; the white blood cells, 11,500; polymorphonuclear leukocytes, 78 per cent; small mononuclears, 12 per cent; large mononuclears, 9 per cent, and transitionals 1 per cent. A throat culture showed *Streptococcus viridans* in practically pure culture. Repeated examinations of the urine were negative for acid-fast bacilli. Fluid from pustules did not show any fungi, and a culture of the blood was negative.

On December 9, the patient was admitted to the ward of the dermatologic service for observation, study and treatment. A definite diagnosis was not made, although the possibilities of a tuberculid or erythema multiforme with destructive features was entertained. She was placed on colloidal baths and massive wet

Fig. 9.—Close-up of elbows, forearms and hands, showing crusted ulcers.

boric dressings, under which the ulcerations involuted. The patient was discharged, December 22, with instructions to return in one month for further observation. During this first period of hospitalization, she received in addition to the local therapy, 3 minims of solution of potassium arsenite, twice daily, cod liver oil and a high caloric diet.

On her return, the patient again entered the hospital for a two months' stay. During this period, she was placed on the same treatment as before, except that potassium permanganate dressings were applied to the ulcerative lesions. She also received six ultraviolet light treatments. A submaxillary abscess developed, was incised and drained. Cultures of the pus showed *Streptococcus hemolyticus*. The skin lesions gradually involuted, and at this time, on account of the recurrence, symmetry, grouping (both buttocks, the elbows, knees and feet) and the presence of vesicles, a diagnosis of dermatitis herpetiformis of a severe form was suggested. Some superficial, brightly inflammatory, pinhead-sized pustules appeared over the buttocks, but it was thought that these were chiefly due to the enuresis. They involuted under mercuric chloride dressings, and the application of one-half strength ammoniated mercury.

For the following two months, the patient was transferred to the pediatric service for study directed particularly toward the enuresis. The studies revealed

a spina bifida occulta and colon bacillus pyuria. The latter gradually cleared up under a forced fluid intake and acid sodium phosphate by mouth.

After her discharge, the patient was not seen again for almost one year. Up until this time no new lesions had appeared, but the older ones had persisted, and more recently those over the knees had increased in size and had become quite painful. Examination revealed numerous scars of previous lesions, both atrophic and hypertrophic. Several lesions about the ankles appeared to be involuting, and over the buttocks there were many bluish-red plaques, which were covered by crusts, varying in size from that of a pea to that of a dime and larger. Over both knees there were superficial ulcerations at the site of old lesions. The right knee, in addition, showed a moderate amount of swelling, and to palpation this was quite tender, and gave the sensation of fluctuation. During her absence from the hospital, the patient had used only colloidal baths, and she was desirous of carrying on the treatment at home in this manner, which she was permitted to do.

Three months later she again returned, and presented numerous papulovesicular and vesicopustular lesions, which varied in size from that of a pea to that of a bean, and in many areas became confluent and crusted. These were surrounded by a bright zone of erythema. The sites of predilection which were involved were those of pressure, namely, the shoulders, the sacral region, the buttocks, backs of the legs, extensor surfaces of the elbows, dorsa of the hands and fingers, the knees and ankles. Few lesions were present on the anterior trunk. The patient looked decidedly pale and was admitted to the hospital where she has remained until the present.

During this period of hospitalization, new lesions continued to appear and involute. One of the striking features of many of these was that they became hemorrhagic, and some of them were even primarily so (fig. 10). The ulcerated lesions would heal slowly, and those lesions which became hemorrhagic were extremely tender to palpation.

Various types of treatment were instituted. Locally, these consisted of baths and wet dressings, either boric acid or potassium permanganate, and exposure to ultraviolet light, both air and water cooled. She received also Asiatic pills, cod liver oil and a high caloric diet. Increasing doses of tuberculin, autohemotherapy and intravenous injections of gold and sodium thiosulphate together with lipoiodine-Ciba, one tablet daily, were also tried.

Laboratory Observations.—The blood Wassermann reaction and cultures of the blood were negative. The latter were made on dextrose broth, liver extract and brain infusion mediums, and the glycerin and lactose agars that Lutz [11] employed. In ten examinations, the hemoglobin varied between 55 and 78 per cent; the total number of red cells between 3,330,000 and 5,410,000; the total number of white cells between 6,650 and 15,800; the polymorphonuclears varied between 49 and 73 per cent; the total lymphocytes between 22 and 46 per cent; the transitionals between 0 and 6 per cent; the eosinophils between 0 and 4 per cent, and the basophils between 0 and 2 per cent. In the majority of examinations, the red cells showed a slight achromia, and the platelet count was normal or slightly diminished. The clotting time varied between normal limits. Examination of the urine was always negative, except during the time of pyelocystitis, when it contained albumin, blood, pus, casts and colon bacilli. A culture of the pus from the right submaxillary abscess yielded a *Streptococcus hemolyticus*. Culture of the lesions yielded on one occasion a hemolytic streptococcus, *Staphylococcus aureus* and a diphtheroid. On another occasion a *Streptococcus hemolyticus* grew in pure

culture. Examination of smears from the lesions was negative for acid-fast organisms and fungi, and there was no fungus growth obtained on Sabouraud's medium. The reaction to the tuberculin test was repeatedly negative, and there was no local or general reaction to increasing doses of old tuberculin. Guinea-pig inoculation of an excised inguinal gland was also negative. Roentgenograms of the chest were repeatedly negative for evidence of Koch infection, and at the time of the submaxillary abscess a roentgenogram of the jaw did not show any bony pathologic process. Intradermal injection of fluid obtained from a vesicle, rapidly produced a pustule which broke down in the center, and ulcerated.

Fig. 10.—Close-up of sole, showing hemorrhagic macules and papules.

After months of study it seemed that the lesions evolved in a definite cycle. The hemorrhagic lesions, which were either petechial or papular, would either involute spontaneously, or become necrotic and ulcerate. The vesicular lesions would rapidly become pustular and in some cases hemorrhagic, and then ulcerate and crust over. The infiltrated plaques, which occurred chiefly over the buttocks, would persist for a long time, but finally would also undergo central softening with crusting and ulceration.

Histologic Examination.—Six biopsies were taken from various places including all types of lesions. An inguinal gland was also excised for examination, but showed only chronic lymphadenitis without any evidence of tuberculosis.

The hemorrhagic papule presented a structure singularly like that seen in angiokeratoma. The striking feature (low power) was a large intra-epidermal hemorrhage (fig. 11). This hemorrhage occupied for the most part the upper portion of the rete; it was well encapsulated, and covered with horny epithelium. There was also seen a marked dilatation of the blood vessels in the upper corium, and a striking dilatation of the deeper arterioles and veins. Immediately subjacent to the hemorrhage and occupying the papillary layer there was a diffuse infiltration which consisted of lymphocytes and a large number of cells of an epithelioid type. This infiltration was not like that of an ordinary acute inflammatory process. As in angiokeratoma, diapedeses and lymphocytic infiltrations could be seen here and

Fig. 11.—Intra-epidermal hemorrhage. Note the resemblance to angiokeratoma.

there in the epidermis and the papillae from the markedly dilated blood vessels. There was also considerable free hemorrhage in the upper portions of the corium immediately below the greatest diameter of the intra-epithelial hemorrhage.

The vesicopustular lesions (fig. 12) were seen to be made up of distinctly rounded intra-epithelial abscesses occupying the upper portion of the cutis. The remainder of the section was characterized by an acute polymorphonuclear leukocytic infiltrate with free hemorrhage in the upper portion of the corium. The picture in the corium was that of diffuse abscess formation. That this diffuse purulent exudate was coming from below and exerting pressure was evidenced by the complete flattening of the interpapillary tufts (fig. 13). Considerable fibrin was also seen, and the picture was not unlike that seen in deep-seated streptococcus infection or phlegmon.

The plaquelike lesions (fig. 14) revealed themselves as early abscesses and necroses extending from the subpapillary layer almost to the coil glands. The abscesses were sharply limited, and showed definite central softening and considerable free hemorrhage. Just outside the mass of abscess in the plaquelike lesions an enormous dilatation of the blood vessels was seen throughout the corium. Sections taken earlier (fig. 15) in the same type of lesion showed striking vascular dilatation and both a diffuse and perivascular leukocytic infiltration throughout the corium. There were no vessels seen to be thrombosed.

Stains for elastic tissue showed striking absence of elastica in the involved areas, but the massing of the elastic fibers around abscess cavities indicated that

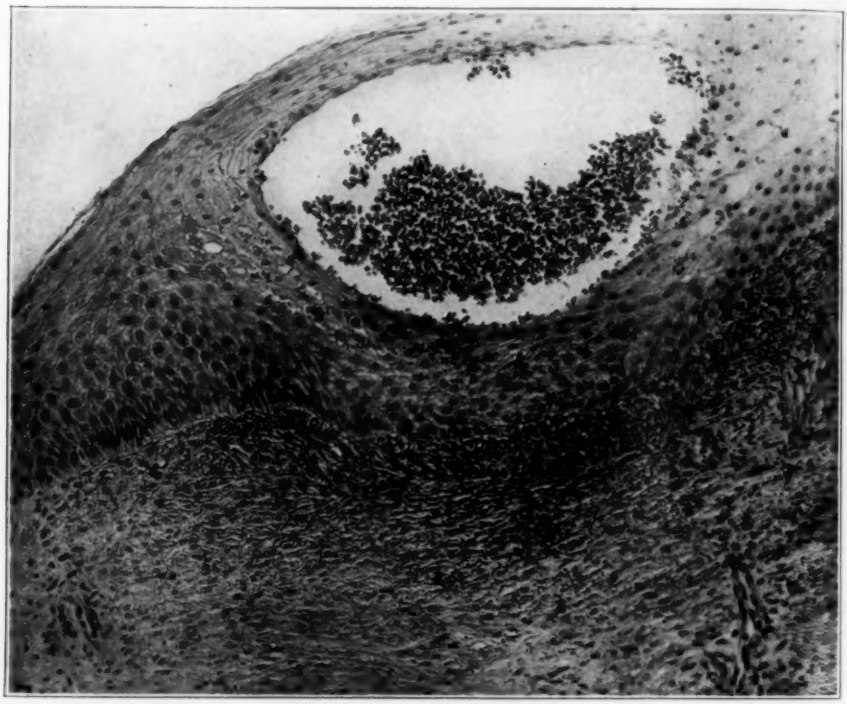

Fig. 12.—Vesicopustule (high power). Note the infiltrate and free hemorrhage high up in the corium.

the elastica changes were secondary to the abscess formation rather than a primary change.

To sum up the histologic observations, apparently the condition was a severe deep-seated infection of an acute purulent type, the vesicopustular lesions being the more superficial, and because of their location, apparently breaking down more rapidly. The deeper seated lesions, softening somewhat more slowly, were more destructive, and gave rise eventually to the extensive scars that were characteristic of the clinical picture.

The histologic structure pointed to a septic or embolic process which was brought out clinically by the rise in temperature with each new attack, the leukocytosis and the continuous croplike nature of the exacerbations.

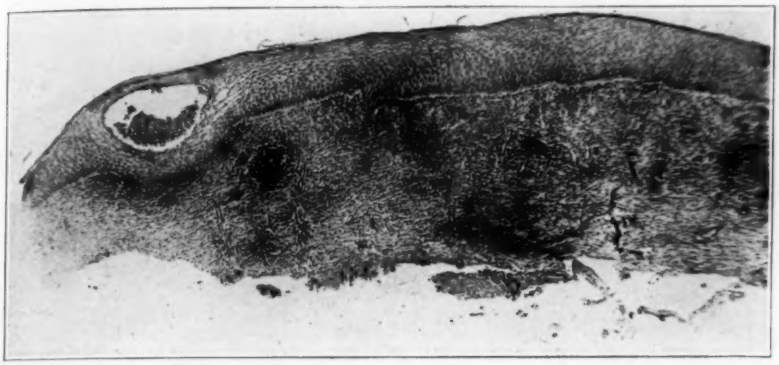

Fig. 13.—Vesicopustule (low power). Compare with figure 5. Note the abscess formation in the corium and the flattening of the interpapillary tufts.

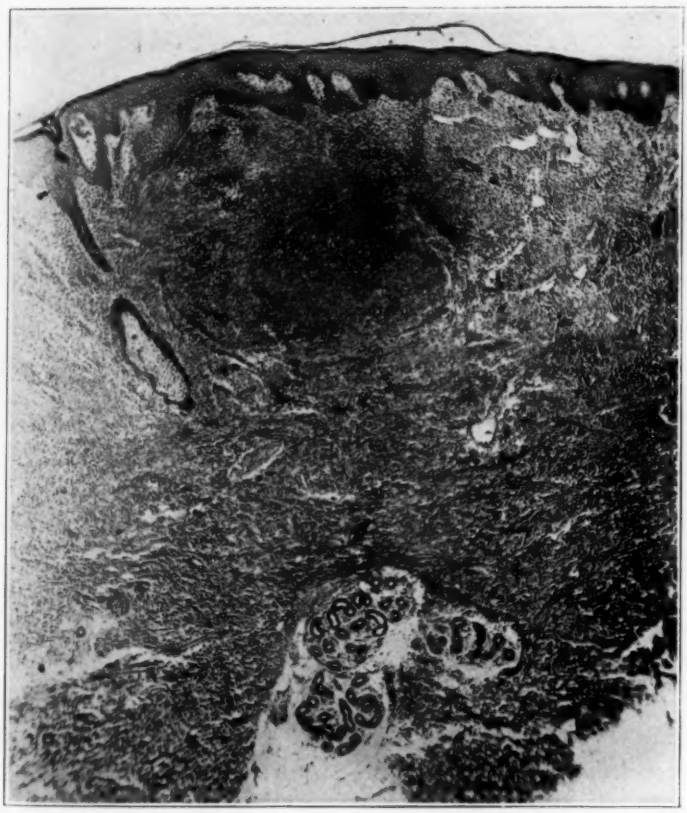

Fig. 14.—Plaquelike lesion, showing abscess formation and free hemorrhage.

SUMMARY OF CASE

A girl, aged 11, for three years and three months has been afflicted with an acutely exacerbating dermatitis, involving by predilection the back, extensor surfaces of the elbows, the dorsa of the hands and fingers, the knees, legs and feet, including the palms and soles. The eruption was polymorphous in character, presenting as papules, vesicles, pustules, nodules, ulcers and hemorrhagic lesions, the last being a striking feature. Although the course was chronic, it was characterized by periodic acute exacerbations, which were accompanied by a slight

Fig. 15.—Plaquelike lesion (high power), showing vascular dilatation and diffuse and perivascular leukocytic infiltration.

rise in temperature, and the general health of the patient was little affected, save for anemia. There were no subjective symptoms associated with any of the lesions, except the ulcerated and hemorrhagic ones which were quite tender to palpation. The condition involuted and recurred regardless of the type of treatment that was directed toward it. The right submaxillary and the inguinal glands enlarged and suppurated. Roentgenograms of the chest and tuberculin tests were repeatedly negative, and there was no history of tuberculosis in the family, and no tuberculous contacts.

CONCLUSIONS

1. Under the title of "dermatitis nodularis necrotica" there are recorded in the literature two types of cases.

2. Clinically, these are all characterized by polymorphous eruptions (macular, papular, papulopustular, papulonecrotic, hemorrhagic and ulcerative), involving by predilection the extremities.

3. The first group is associated with visceral tuberculosis, and is possibly related to this disease.

4. A smaller group exists in which tuberculosis can definitely be excluded as a factor.

5. The tuberculous group should be definitely separated as examples of cases of unusual skin tuberculosis.

6. The smaller group in which tuberculosis can be definitely excluded both clinically and histologically constitutes a rare dermatosis to which the name suggested by Klingmüller [2] can properly be applied.

7. From a prolonged clinical study as well as the histologic observations, it is suggested that this is an unusual form of sepsis, in spite of the negative blood cultures. The constant finding of *Streptococcus hemolyticus* in the lesions as well as the lymph glands suggests this organism as the etiologic factor.

ABSTRACT OF DISCUSSION

DR. STILLIANS, Chicago: In a case that came under my observation I was impressed by the striking clinical appearance of this disease, or symptom-complex, whichever it may be. I had all sorts of difficulties in what little I tried to do but never found anything indicative of tuberculosis, although the work was far short of the demonstration of the absence of tuberculosis.

PROFESSOR JADASSOHN, Breslau, Germany: I have observed one case of this disease, also in a young girl, 5 or 6 years.[1] It was not possible to find the cause of the disorder. The patient had an old tuberculosis in the lungs but it had been cured for a long time, and while all kinds of examinations were made the cause of the eruption could not be found. For a certain time I thought it might be an extraordinary form of tuberculids, and I even sent her to Leysin. All efforts to cure the disease were without result. A short time before I left Breslau I received a letter from this girl, and after a year in Leysin there had been no effect on the disease. The eruption comes and goes, always in the same way. The general health of the patient is quite good. I never saw a similar case in which I could establish the diagnosis of tuberculid. Therefore, personally I believe the disease is not yet to be diagnosed.

DR. CANNON, New York: A few months ago I had a case of this type, although the lesions were much more extensive and involved the mucous membranes of the mouth as well as the cutaneous surfaces. Smears and cultures from the ulcers showed a ***Streptococcus viridans*** although the blood cultures were negative. At necropsy, an extensive pancarditis, hepatitis, and splenitis were present and *Strep-*

1. Jadassohn: Centralbl. f. Haut u. Geschlechtskrankh., vol. 29, p. 762.

tococcus viridans from these organs were grown in culture. Owing to the marked involvement of the blood vessels as shown in sections taken from the skin lesions and the affected organs it was first suggested that the patient had a periarteritis nodosa, but the diagnosis was later changed to that of a vascular disease due to streptococcic infection. A few days after I saw the patient I saw a child suffering from acute articular rheumatism and pericarditis with numerous subcutaneous and cutaneous nodules over the skin, some of which were bluish. One of the tumors when removed showed a subcutaneous abscess, cultures from which were diagnosed as *Streptococcus viridans.* In neither case could the organism from the blood stream be cultured prior to death.

DR. SCHOLTZ, Los Angeles: I would like to know why such a condition should be called "dermatitis nodularis necrotica." It is cutaneous and nodular, but it is not a dermatitis.

DR. FOERSTER, Milwaukee: At the last meeting of the Mississippi Valley Dermatologic Conference a patient was presented for diagnosis with a papulopustular eruption for which Dr. Wile offered the diagnosis of dermatitis nodularis necrotica. While not conforming sufficiently to the features of Dr. Duemling's case to be classed with it, there was a similarity that justifies reference to it. The chief features of this case were the symmetrical distribution of the lesions and their croplike appearance, both suggestive of dermatitis herpetiformis, the persistence of the individual papulopustules as small and discrete lesions even after they became necrotic, the marked eosinophilia in the subepidermal infiltrate and the persistently negative smears and cultures. It appears that in obscure cases of this type, in which tuberculosis is often suspected, the streptococcus is worthy of consideration as a possible etiologic factor.

DR. WEIDMAN, Philadelphia: I wish to mention a case [2] of acne varioliformis simply to get it into the records in connection with this paper. There is a striking resemblance between that case and the one under discussion, and in that case the streptococcus was isolated from the lesions. The patient had a phlyctenular keratitis, which the ophthalmologists refer to as tuberculosis; yet this disease was not demonstrated in any of the viscera. May I ask what the differential diagnosis is between the disorder Dr. Duemling describes and acne varioloformis?

DR. DUEMLING, Ann Arbor, Mich: The fact that the lesions appeared in crops a week or ten days or two weeks apart, and that they were accompanied by a rise in temperature and increase in the leukocytes, led to the belief that some septic or embolic process was going on. In this case there was no response to treatment, as Professor Jadassohn indicated. The condition did not affect the general health of the patient. She carried along quite well, except for a slight anemia. Blood cultures were repeatedly negative. On seven or eight occasions at different times I attempted to find organisms in the blood stream, but was never able to find anything with the special mediums with which Lutz found his gram-negative organism. I do not know that there can be a better term for this condition unless more is known about it. It is a dermatitis, with considerable inflammatory reaction about the lesions, particularly the vesicopustular ones. It is nodular, the nodules being the size of a cherry or larger. These nodules and the other lesions also often break down into necrotic, gummous ulcers.

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2. Strumia, M. M.: Experimental Acne Varioliformis, Arch. Dermat. & Syph. **10**:702 (Dec.) 1924.

CIRCUMCISION

ITS VALUE IN THE TREATMENT FOR CHANCROIDAL LESIONS OF THE MALE GENITALIA *

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The dermatology service of Cleveland City Hospital admitted 1881 adult male patients to its wards from July 1, 1924 to Jan. 1, 1929, an interval of four and a half years; 1098 of these cases presented penile lesions; 537, or 49 per cent, of these genital lesions were chancroidal infections. The average age of the patients with chancroidal lesions was 27. Three fifths of the cases occurred in negroes.

The service has had recourse to all the time-honored local and constitutional therapeusis, such as soaks, irrigations, iodoform, caustics, electrocautery, hygiene and rest in bed. The lengthy tedious treatment offered, at best, 50 per cent of cases of complicating suppurative inguinal adenitis which the patient either brought in with him or developed under therapy. More than 26 per cent of the total number of suppurating glands developed during this type of therapy. Gradually sufficient evidence was accumulated to formulate certain axioms:

The smaller and more inaccessible the ulcers are to therapy, the more likely the occurrence of buboes.

Conversely, the larger and more accessible to therapy the lesions are, the less the incidence of buboes.

Caustics or actual cautery predispose to the development of adenitis.

Lesions so situated as to produce phimosis and poor external drainage, are more apt to initiate adenitis than are lesions on the cutaneous surface of the prepuce or the shaft of the penis.

These facts, it was reasoned, must be dependent on the lymphatic drainage provoked in each case. Just as surely as the lymphatic drainage was overtaxed, suppurative inguinal adenitis was inevitable. On Sept. 19, 1925, it was decided to abandon the traditional customary teaching, never to resort to surgical procedures in tissues infected with Ducrey's bacillus, and the ulcerated prepuce in a young white male patient was amputated. The patient was discharged twenty days later without the occurrence of any complication.

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* Submitted for publication, July 15, 1929.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 11, 1929.

* From the Department of Dermatology and Syphilology of the Western Reserve University and Cleveland City Hospital.

In 1858, Ricord [1] wrote of these cases: "The benefit to be derived from operation does not compensate for the inevitable danger of inoculation of the wound and forced extension of the chancre." The profound influence of Ricord's teachings in this matter can still be felt in the practice of most men. In the past forty to fifty years, however, several clinicians have had the courage to doubt the infallibility of this premise. Aubert,[2] in 1882, asserted the frequency of healing by first intention in circumcision of patients with chancroid. Ten years later, Salsotto [3] operated on five such patients and had only one case of inoculation. Carle,[4] in 1904, reported treatment by early circumcision in fourteen cases of chancroidal lesions of the prepuce. Only one of these cases showed inoculation. This worker had comprehensive indications for circumcision. Later he had a series of seven cases with marked phimosis or paraphimosis; one in this group had a severe inoculation and one had a marked systemic reaction. In this country, Bellenger [5] in 1902 recorded the first circumcision done as treatment for chancroid. In 1918, Van Winkle [6] recorded healing by first intention in twenty-four of a series of twenty-eight cases. Newman,[7] in 1920, treated nine patients surgically without any development of lymphatic complications.

TREATMENT IN PRESENT SERIES

Altogether, circumcision has been performed in 171 cases of chancroid. In the early cases sutures were used. The 137 patients in this group averaged 27.25 hospital days. In 34 later cases, clips superseded sutures. These patients averaged 26.25 days' sojourn in the hospital. The stay in the hospital after circumcision in cases of simple chancroid averaged 18 days; 366 patients were treated without circumcision, and in these medically managed cases, the stay averaged 23.4 hospital days. In not one case in the circumcised series did buboes develop.

From this experience, conclusions are drawn that definitely establish the value of circumcision in the treatment for chancroids, because:

1. There were no complications, such as buboes, balanitis, phagedena, and phlebitis of the dorsal vein.

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1. Ricord, P.: Leçons sur le chancre, Paris, 1858, quoted by Carle.

2. Aubert, P.: De la réunion immédiate dans l'opération du phimosis compliquant le chancre simple, Lyon méd., Feb. 26, 1882.

3. Salsotto: Sulla opportunita di operare il fimosi che complica l'ulcera venerea, Morgagni, April, 1892, p. 247.

4. Carle: Le traitement chirurgical du chancre molle, Semaine méd. **24**:273, 1904.

5. Bellenger, P. L.: Circumcision for Chancroids and Other Causes, N. Orleans M. & S. J. **55**:347, 1902.

6. Van Winkle, J. S.: Circumcision in the Presence of Chancroids, U. S. Naval M. Bull. **12**:712, 1918.

7. Newman, S.: Virginia M. Monthly **47**:311, 1920.

2. The likelihood of establishing an early diagnosis of syphilis by dark-field examination of ulcers rendered accessible by removal of the prepuce, is increased. Mixed infection, syphilis and chancroid, occurred in 15 per cent of the total group of patients exhibiting penile lesions.

3. The accessibility of the ulcers makes the care of the lesions themselves much easier.

What was not established by means of radical treatment was a spectacular decrease in the period of hospitalization. I did not feel too chagrined over this, though, because no attempt was made to develop a group of cases in which early discharge was made a matter of concern for establishing the value of circumcision. Many of the patients remained in the hospital longer than the chancroids required, for the treatment of concurrent syphilis. Circumcision was usually delayed for varying periods to permit establishment of a complete and definite diag-

A B

Fig. 1 (T. C.).—*A*, appearance of lesions eleven days following circumcision; *B*, (J. B.) lesions of the mucocutaneous juncture are healed, twenty-six days following circumcision.

nosis, to render the field safer for the surgeon and to clean up secondary infection, particularly streptococcic. With increased experience the technic was improved and still is improving; this must result in a shorter stay in the hospital. Many patients, admitted as they are to a municipal hospital, must be maintained until the draining buboes with which they entered are healed.

TECHNIC

Early and complete diagnosis is held to be of paramount importance. To that end, patients are subjected to dark-field examination on the first three consecutive days of their hospital stay. Diagnosis of chancroidal lesion is established by the positive observations of stained smears from the purulent discharge and by autoinoculation in certain selected cases or by the negative observations of dark-field examinations and serial Wassermann tests of the blood. All patients with

chancroid, except those in whom the lesions are confined to the shaft of the penis, are circumcised.

The patient is prepared by means of ¼ grain (0.016 Gm.) of morphine sulphate and 1/150 grain (0.004 Gm.) of scopolamine given subcutaneously, about fifteen minutes before he undergoes the operation. The field is shaved and prepared

Fig. 2 (A. C.).—Chancroidal lesions of the entire prepuce; clinical appearance on admission.

A B

Fig. 3.—*A*, same patient shown in figure 2, four days following admission. Note the extension of the lesions under the old type of therapy; *B*, same patient, twenty days following circumcision; the patient was discharged the same day.

with soap, ether and alcohol. A local anesthetic is administered with a 2-inch, 21 gage needle, inserted at the midpoint of the dorsal aspect of the penis, close to its root; 2 per cent procaine hydrochloride is injected. The needle is gradually deflected as far to the left as possible during this procedure, then brought back

to the starting point but not withdrawn, and deflected to the right. The needle is again brought to the midline and pushed down the dorsum of the shaft as far as possible toward the glands. The whole procedure is performed through the original puncture wound. The same procedure is followed with the needle in a similar midpoint of the ventral surface. Sufficient procaine hydrochloride is injected subcutaneously to cause considerable swelling of the tissue. Epinephrine is not used. The vicinity of the frenum is most sensitive; a similar plan of infiltration, therefore, is followed with one dorsal and one ventral injection at the free border of the prepuce. The combination of morphine-scopolamine and local

Fig. 4 (B. J.).—Clip method of circumcision.

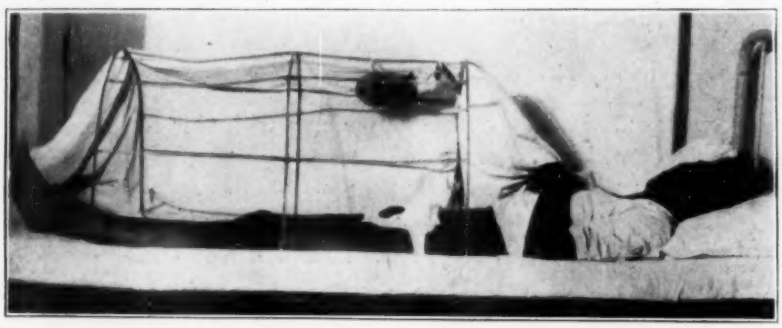

Fig. 5.—Postoperative care of same patient as in figure 1.

anesthetic is so satisfactory that patients occasionally fall asleep during the operation.

With the penis anesthetized, the field is prepared by scrubbing the shaft, prepuce and glans with a hand brush and soap and water. It is usual for the ulcers to bleed. The dorsal slit is employed only in cases of marked phimosis with an adherent prepuce and paraphimosis. The guillotine method is the method of choice. A hemostat is placed at the midpoint of the free edge of the prepuce on the dorsal surface and another at a similar point on the ventral aspect in the vicinity of the frenum. By strong traction on the hemostats the prepuce is pulled down as far as possible; during this procedure the coronal sulcus becomes visible or is easily palpable. A hemostat is now applied parallel to the coronal sulcus and

as close to the glans as possible. The prepuce is amputated by cutting against the guiding hemostat and on the proximal side. No attention is paid to the situation of the chancroidal lesions. Only arterial hemorrhage receives attention at this time, and free bleeding is encouraged. The edges are trimmed to make a smooth border. The free edge is thoroughly scrubbed as before, and then care is given to secure complete hemostasis by tying off all vessels. Formerly the skin and mucous membrane were coapted with sutures. This has now been discontinued, for the sutures sloughed out too readily or pulled out or broke with erections. Further, it seemed that the through and through course of the sutures served as a ready avenue for the transfer of infection. Coaptation is now secured by ordinary skin clips which are put in to the number of ten or twelve and never farther apart than a fourth of an inch (0.63 cm.). No attempt is made to insert a clip where the tissue is already necrotic. Special attention is paid to buckling this collar of clips by an extra, transversely placed clip at the frenum.

The patient's thighs are strapped together with 2-inch adhesive tape, a suspensory bandage is applied and the patient is returned to the ward after the field is dusted with iodoform powder. No dressing is applied. All these patients are strictly confined to bed. A cradle is placed on the bed. A bulb with a carbon filament is attached to furnish increased heat continuously. Bromides and chloral hydrate are employed as sedatives.

Twenty-four hours after operation the real postoperative care begins. Hot potassium permanganate soaks, 1-8-10,000, are employed four times a day. The patient is supplied with gauze and advised to remove all débris. A physician performs the debridement every morning. Between soaks, iodoform powder is used. Auto-inoculation, along the line of incision, is never troublesome with this routine. The clips remain in until the incision is healed, whether that be seven or fourteen days. They are gradually removed; those at the dorsal and ventral midpoints are preserved until the last.

SUMMARY

1. One hundred and seventy-one patients with chancroidal infection have been treated by circumcision.

2. Circumcision and chancroidal infection are not incompatible when the operation is performed under hospital conditions.

3. The actual time that the patients spent in the hospital after circumcision has compared favorably with the number of days spent by patients treated nonsurgically.

4. Auto-inoculation, when it occurred, responded to treatment readily.

5. Buboes have developed in no patient treated by circumcision.

6. In many instances the procedure has made an early diagnosis of syphilis possible from what was formerly an inaccessible primary infection.

ABSTRACT OF DISCUSSION

DR. SENEAR, Chicago: I was much impressed with Dr. Rauschkolb's presentation for several reasons. In the first place, I think Dr. Cole and his co-workers are to be congratulated on the attention they have given to chancroid in both its acute and chronic stages. This disease is important in dispensary practice, and

yet from the dermatologic standpoint we are often apt to neglect it. Second, I was impressed with their courage in defying tradition. We have always been forbidden to use surgical procedures in chancroid, and I think they are to be commended on overlooking this and proceeding with their method. I have had no experience with their method, and I think few if any other workers have, but in view of the large number of cases in their series, I think we cannot dispute the value of circumcision in chancroid. I think Dr. Rauschkolb would be the first to agree that unless the details are followed with great care the results would not approach those which they obtained, and if care was not used, possibly the results obtained would lead us back to the old tradition. One thing that stands out more than anything else is the absence of bubo. In my clinic, where chancroid is largely in the genito-urinary rather than the dermatologic department, there is a large percentage of bubo. Dr. Rauschkolb has shown that no case of bubo developed after treatment was begun, whereas there was bubo in 26 per cent of the old cases.

Dr. Dennie, Kansas City, Mo.: Dr. Rauschkolb has done away with one of the old hoodoos with which we have had to contend for many years. The old treatment for chancroid was so hopeless that I think this method will be of great benefit. In our section of the country, we do not have this great percentage of chancroids in penile lesions. It is well known that during the war there was a large percentage. It was my fortune to be the examining officer at Bordeaux, and I saw many cases. Since the war, however, the number has greatly decreased. I think that in my section of the country not more than 10 per cent are cases of chancroid. Chancroid is more common among negroes than among members of the white race. One of the reasons for the increase of chancroid during the war was the failure to control it. Prophylaxis was efficient in gonorrhea and syphilis but would not eradicate chancroid.

Dr. Hooper, Jackson, Miss.: Coming from a section of the country where 40 per cent of the population are negroes, we encounter this condition more than physicians do in any other section represented at this meeting. If we hospitalized a patient for the length of time Dr. Rauschkolb advises for treatment, it would not leave the physician anything for payment for his services; therefore we could employ it only in the charitable hospitals. I should like to know if he would advise or could suggest any type of treatment for ambulatory cases. If the light and the dressing he employs are essential to getting results, this treatment could not be used, of course, in ambulatory cases.

Dr. Harold N. Cole, Cleveland: In carrying out this technic, the work is done by interns. No extraordinary skill is used in the circumcision, but we wish to emphasize the fact that it is a hospital procedure.

Dr. Cannon, New York: I have been much impressed with the splendid results obtained by Dr. Rauschkolb, especially in patients with swelling and edema, when treated by circumcision. I have noticed in my service at the City Hospital in New York that when we have circumcised or made dorsal slits, there followed almost invariably a tremendous amount of swelling and sloughing, occasionally not only of the penis but also of the adjacent skin. We have divided our patients into two groups; those with marked inflammation are treated with hot fomentations and iodoform powder until the acute inflammatory reaction subsides, at which time the circumcision is done. We rarely, if ever, have a following secondary infection or sloughing. In the second group, the chronic cases without edema, circumcision is performed at once. I know of no more valuable medication for chancroid than iodoform.

DR. HARTMAN, San Francisco: On the Stanford polyclinic service at the San Francisco Hospital I have had an increasingly small number of cases of chancroid recently, so few that I have been describing the condition to the students as a disease of filth. This probably explains its large incidence among negroes. I think that with bathing and proper hygiene the disease may disappear. I have been impressed by the fact that the lesion responds to the use of oxygen. I have found that free soaking and application of compresses saturated with potassium permanganate solution have given splendid results. This procedure, coupled with Dr. Rauschkolb's free exposure of the lesions to the air, has been largely responsible, I think, for the good results he has obtained.

DR. RAUSCHKOLB, Cleveland: Many of these patients were hospitalized under the quarantine act of the city. Under those conditions we worked up a method that was applicable. We have had no experience in dealing with this technic in ambulatory cases. The lesions are entirely exposed to the drying action of an electric light bulb, and potassium permanganate soaks, and to the empirically specific action of iodoform powder between soaks, the whole technic working together to produce the results described. Dr. Cannon spoke of the dorsal slit. I wonder whether he means the circumcision complete or with the dorsal prepuce hanging down. We have never done that. We relieve the congestion by a complete circumcision at once, not by a two step procedure.

COCCIDIOIDAL GRANULOMA

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In a total of seventy-eight reported cases of granuloma coccidioides, in which the residence of the patients was known, seventy came from California. Dr. W. M. Dickie,[1] director of public health for the state of California, reported that he had the records of 160 cases. As much of the work in this disease has been done by men from California, the presentation of our cases at the first meeting of the American Dermatological Association to be held in that state seems appropriate.

DIFFERENCE BETWEEN GRANULOMA COCCIDIOIDES AND BLASTOMYCETIC DERMATITIS

There is little need to reopen the discussion as to the identity of this disease and blastomycosis. Practically all who are familiar with it recognize granuloma coccidioides as a distinct clinical entity. While there are both clinical and mycologic resemblances, enough sharply defined points of differentiation, both clinical and mycologic, remain to make each one a disease apart.

Clinically, the nodules of the California disease bear a closer resemblance to the typical, specific tubercle than do the nodules of blastomycetic dermatitis. There is, furthermore, a marked tendency toward the involvement of the lymph nodes in coccidioidal granuloma, while in blastomycosis this is slight. Blastomycosis also usually presents its primary focus in the skin with but slight tendency to become generalized, while in coccidioidal granuloma, though the disease may originate in the skin, there is most often generalization. The lesions of blastomycosis generally present rather abrupt, sloping borders studded with miliary abscesses, an appearance which is not noted in granuloma coccidioides.

Mycologically, the essential difference is that in the tissues *Blastomyces* reproduces by budding while *Coccidioides immitis* reproduces by endosporulation. *Coccidioides immitis* grows much larger than *Blastomyces.* In cultures *Coccidioides immitis* grows as mycelial threads and forms chlamydospores. No large capsulated or budding forms are ever seen, while they are commonly present in cultures of *Blastomyces.*

* Submitted for publication, April 1, 1929.

* Read at the Fifty-Second Annual Meeting of the American Dermatological Association, San Francisco and Del Monte, Calif., July, 1929.

1. Dickie, W. M.: Personal communication to the authors.

Montgomery and Morrow [2] have clearly indicated the differences between the two diseases and their organisms.

REPORT OF CASES

In 1913, one of us (E. D. C.) reported [3] a case of coccidioidal infection of the tip of the nose (fig. 1).

CASE 1.—A man, aged 28, a machinist, was a resident of the San Joaquin Valley. The family history showed that a maternal aunt had died of tuberculosis. The previous cutaneous history was negative, but the general history indicated some cough and loss of weight for the preceding three months. The sputum showed tubercle bacilli.

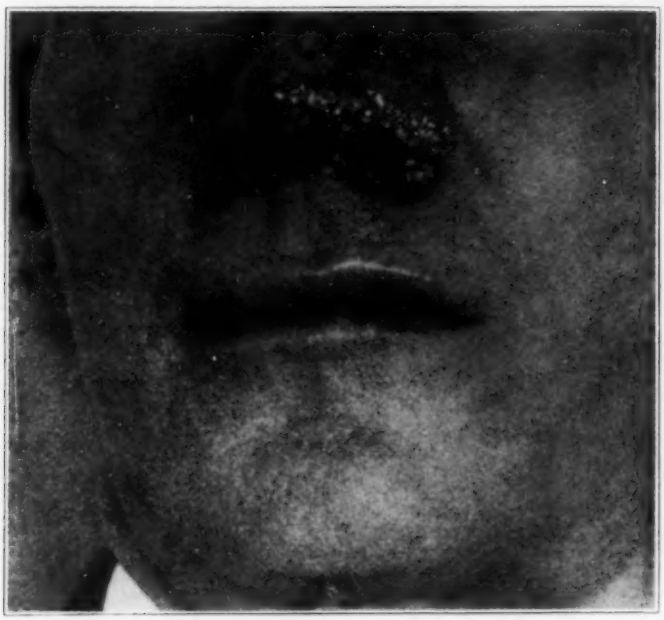

Fig. 1 (case 1).—Coccidioidal granuloma of the tip of the nose.

The skin eruption was first noted by the patient two months before examination as a "pimple" on the side of the nose. When first observed by us it had attained a size of 3 cm. in diameter extending to the upper lip. It was circular and was elevated above the surrounding skin approximately 5 mm. It was violaceous and boggy, and was apparently made up of an agglomeration of papules. Scattered throughout the surface were numerous, superficial pustules. Subjectively, it was painful, tender and intolerant of any save the blandest applications. There was no evidence of scar tissue; neither was there any sign of a tendency to spontaneous repair, nor a suggestion of any verrucous element. The submaxillary lymph node on the corresponding side was markedly enlarged. Smears from the pustules showed doubly contoured cells which were identified by Dr.

2. Montgomery, D. W., and Morrow, Howard: Reasons for Considering Dermatitis Coccidioides an Independent Disease, J. Cutan. Dis. **22**:368, 1904.

3. Chipman, E. D.: The Newer Cutaneous Mycoses, J. A. M. A **61**:407 (Aug. 9) 1913.

Ophüls as coccidioidal fungi. Further search of the sputum again disclosed tubercle bacilli, but no fungi could be demonstrated.

The cutaneous lesions as well as the enlarged lymph node showed marked improvement under the administration of potassium iodide, but what was clinically a laryngeal tuberculosis quickly followed the primary condition. The patient died within a few months after the first observation, and postmortem examination was impossible.

CASE 2.—*History.*—Fred T., a Mexican, aged 26, was referred by Dr. Guerra of Alameda because of cutaneous lesions on the neck, back and finger, swollen cervical and axillary glands and discharging sinuses over the outer aspect of both thighs. The family history was unimportant, there having been no similar disease or tuberculosis in any of the relatives. The patient's past history also revealed nothing of consequence.

Fig. 2.—Fairly firm verrucous papules on the neck. On the finger they have fused into one plaque. They are all dry and suggestive of tuberculosis verrucosa cutis.

The patient went to Oakland in March, 1925, and was employed in a cotton mill. The following August he noticed a swelling of the left cervical lymph nodes. Shortly after this an abscess appeared over the left scapula. This was incised but refused to heal and persisted in draining. In November, another abscess appeared in the right cervical lymph nodes. In June, 1926, the cutaneous lesions to be described appeared on the right side of the neck. Six weeks thereafter the eruption spread to the second finger of the right hand. Some time during 1926, an abscess developed posteriorly over the left hip. This was opened and was still draining. In October, 1927, an abscess developed anteriorly over the left hip and was still draining. At the same time lesions appeared on the toes. In July, 1928, an abscess developed over the right hip posteriorly but had recently healed. During this time, the patient had worked steadily and had no complaints except

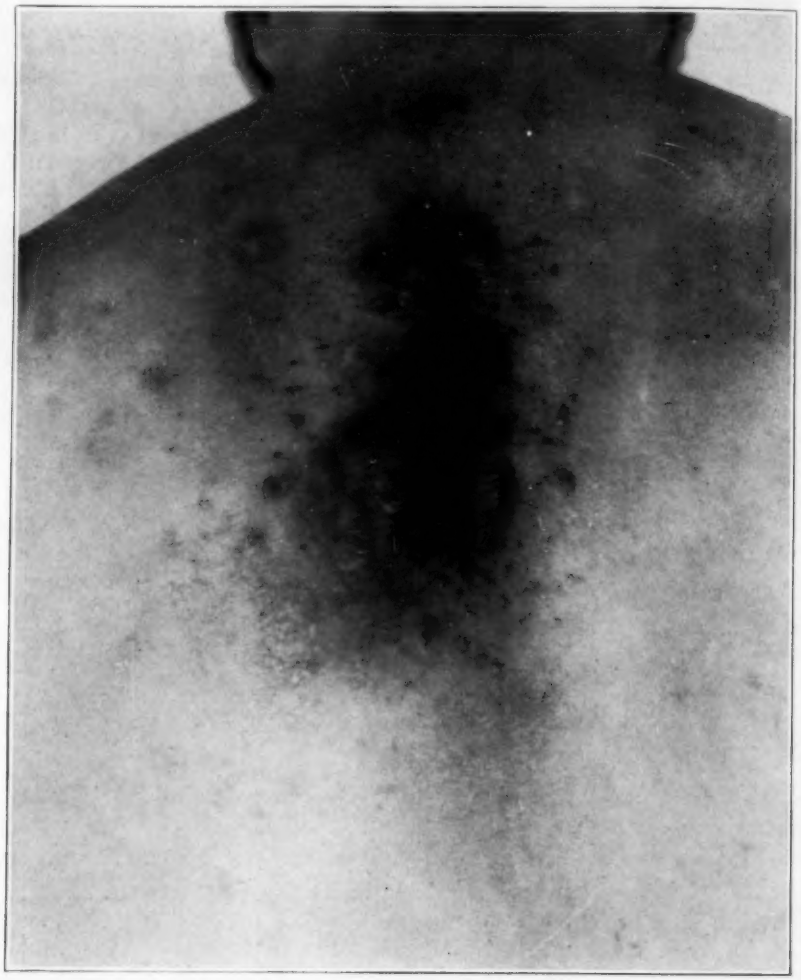

Fig. 3.—Papules and nodules running together to form a solid sheet. The larger ones are verrucous.

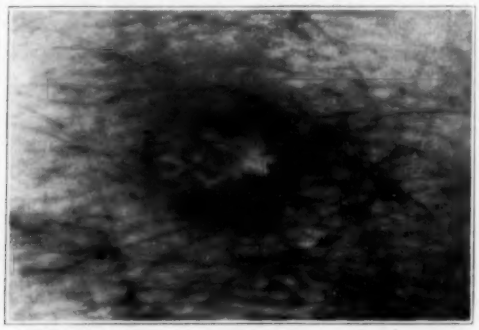

Fig. 4.—Large nodule in the patient's skin. The light points are scales, not pus.

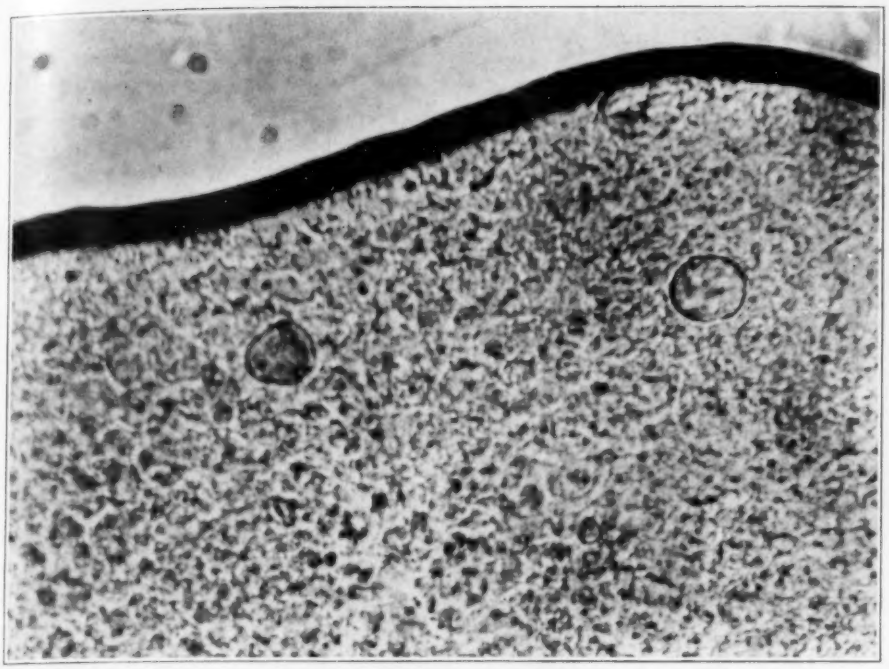

Fig. 5.—Young, immature forms of coccidioides immitis.

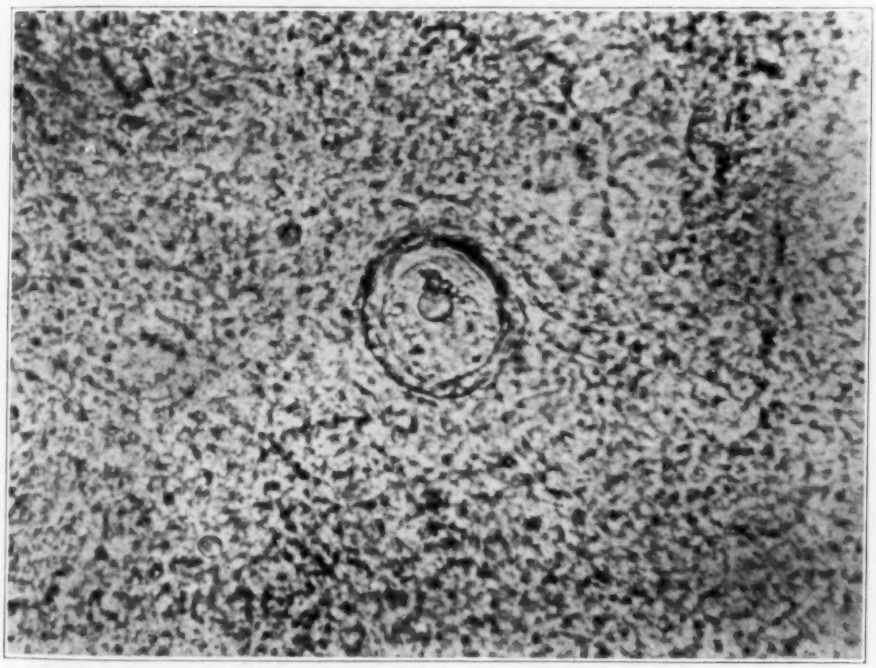

Fig. 6.—Typical adult coccidioides body from pus from the patient The double-contoured capsule shows plainly, also an endospore.

pain and tenderness when the abscess developed, and also some weakness. He had no symptoms referable to the lungs.

Examination.—Physical examination disclosed that he was fairly well nourished, with a rather marked pallor. The eyes, ears, nose, mouth, throat, lungs, heart, abdomen and nervous system showed nothing worthy of note. The blood pressure was 126 systolic and 80 diastolic. Below the right ear (fig. 2) there were many reddish-brown papules varying in size from that of a pinhead to that of a

Fig. 7.—Coccidioides immitis growing on dextrose-peptone-agar, fourteen days after inoculation with the patient's pus.

split pea. The initial lesions were small firm papules showing no vesiculation or crusting. They gradually enlarged or coalesced with others to form rather rough, almost verrucous patches the size of a split pea. These were generally dry and crusted, but at times there had been a slight seropurulent discharge from some of them. On the dorsum of the second finger of the right hand (fig. 2), there was a slightly violaceous plaque about 1 cm. in diameter, somewhat indurated and having rather sharp margination. It was elevated about 2 mm. above the level of the skin; its border contained no miliary abscesses. In the interscapular

region (fig. 3), there were many lesions similar to those on the neck. They were so numerous that they had almost fused into a large sheet. The largest single lesion occurred on the thigh, and is shown in figure 4. Subjective symptoms were practically absent.

Laboratory Observations.—The Wassermann reaction of the blood was negative on several occasions. The blood showed: red cells, 5,900,000; hemoglobin content, 30 per cent; leukocytes, 8,200; polymorphonuclears, 64 per cent; lymphocytes, 32 per cent; mononuclears, 3 per cent, and eosinophils, 1 per cent.

It should be noted that there was no marked eosinophilia as has been seen in other cases.[4] On the other hand, a marked secondary anemia was present.

The results of several urinalyses were essentially negative.

Blood culture gave no growth on ordinary mediums or on Sabouraud's dextrose-peptone-agar. Unfortunately, this was not taken before the patient had received considerable intravenous therapy.

An intradermal tuberculin test was negative.

The cerebrospinal fluid was not examined on account of the fear of carrying infection in from the skin.

Mycology and Cultural Examinations.—Pus from the sinuses leading into the left ilium was mounted in 20 per cent potassium hydroxide. Untreated smears were also examined. The organisms as seen in figures 5 and 6 were found. They varied in size from about 10 to 40 microns. The smaller ones contained a clear substance (fig. 5). Some of the larger ones contained endospores (fig. 6). Neither budding forms nor mycelis were seen.

One week after the pus was planted on dextrose-peptone-agar a hazy growth could be seen. This spread rapidly, became whiter and thicker and in two weeks had attained the size shown in figure 7. This culture was milky white and shaded off rather hazily at the borders instead of being clearcut. The aerial hyphae were rather high, generally about 6 mm. Many of them closely resembled a tiny tree, there being a single trunk capped by a cottony ball. Older cultures were more creamy in color.

Smears from the growth on dextrose-peptone-agar three days after inoculation are shown in figure 8. It can be seen that there were no spherical, budding or endosporulating forms present. The mycelial threads were seen to be growing out from the spores. Individual spores from old cultures are shown in figure 9.

Inoculations into Guinea-Pigs.—A male guinea-pig was inoculated subcutaneously with fresh pus. Thirty days later bilateral swelling of the inguinal glands was present. The animal was killed on the fiftieth day, and autopsy was performed. Both inguinal glands were caseous and there were sinuses present which discharged on the skin. The liver showed several necrotic areas. All the other viscera were normal. Organisms identical with those shown in figures 5 and 6 were found in the caseous inguinal glands. One other guinea-pig was inoculated with pus from the first animal on Jan. 11, 1929. On February 20, one of the tests had increased to triple its normal size.

Biopsy.—A small section of skin was removed from the patient's neck and included a typical early papule. It was stained with hematoxylin-eosin. The stratum corneum (fig. 10) was normal and the stratum granulosum was thinned to one layer of cells. The rete showed slight acanthosis, especially around the follicles. Many of the cells of the rete showed intercellular edema. No epidermal abscesses were seen. This was in striking contrast to blastomycosis. Montgomery, Ryfkogel and Morrow[4] made note of this fact long ago.

4. Montgomery, D. W.: Ryfkogel, H. A. L., and Morrow, Howard: Dermatitis Coccidioides, J. Cutan. & Genito-Urin. Dis. **21**:5, 1903.

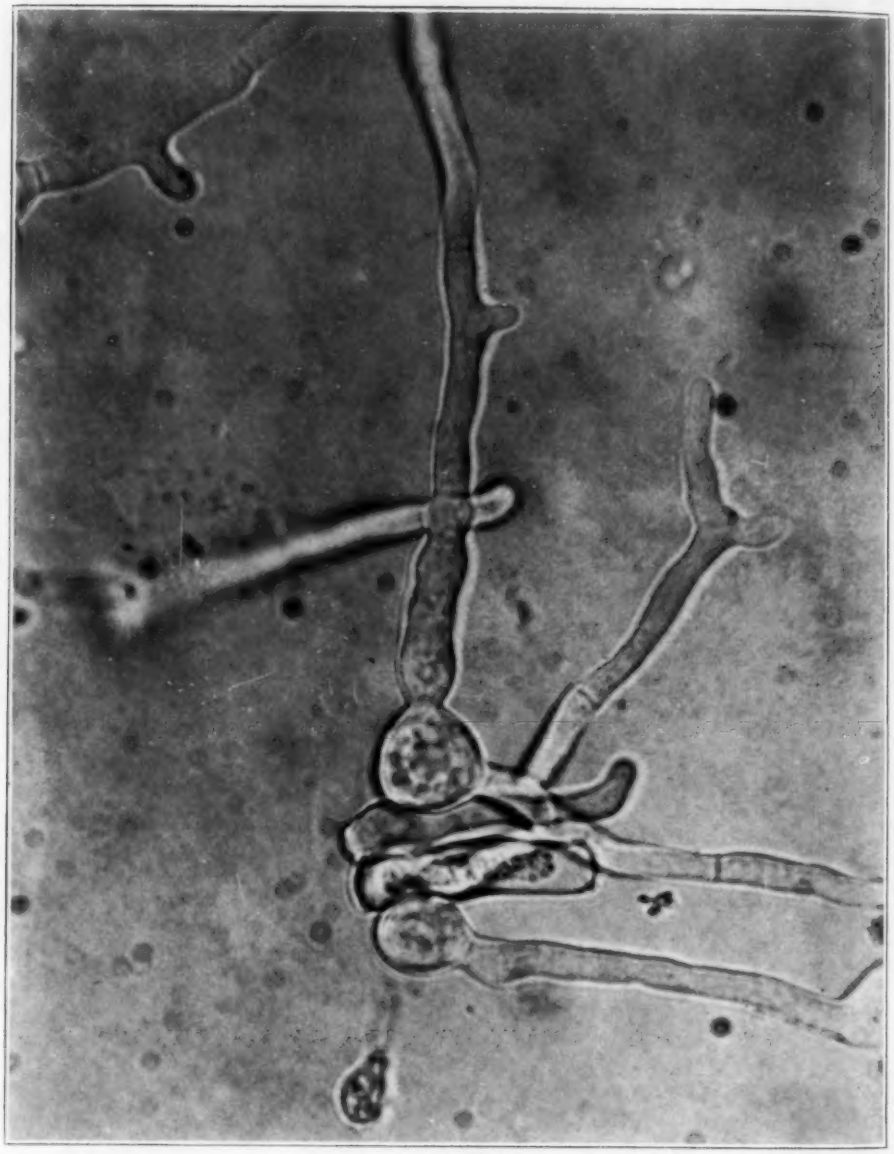

Fig. 8.—Growth of coccidioides immitis on dextrose-peptone-agar. The mycelial threads can be clearly seen growing out of the spore.

The corium was almost filled and disorganized by extensive sheets of cellular infiltrates. This was especially marked deep in the corium but was seen to a lesser degree in the papillae. The infiltration was dense around the sebaceous glands (fig. 11). There was no definite tubercle formation. This infiltrate (fig. 12) was composed mainly of plasma cells. (A photomicrograph of David Davis's case showed plasma cells in abundance.) A few polymorphonuclear leukocytes and epithelioid cells were present. There were a few giant cells, one of which contained a coccidioides cell showing endosporulation (fig. 13).

Intradermal Tests.—Through the courtesy of the California State Hygienic Laboratory we were able to obtain two antigens prepared from bouillon cultures of two known strains of *Coccidioides immitis*. These had been prepared by filtering the bouillon culture through Berkefeld filters and so probably represented

Fig. 9.—Single spores from an old culture.

an exotoxin. The patient received 0.2 cc. of each intradermally. Physiologic solution of sodium chloride was injected as a control. Twenty-four hours later the control was normal (*C*, fig. 14), but large wheals were present at the sites of injection of both antigens (*A* and *B*, fig. 14).

Positive intradermal tests have been reported previously by David Davis [5] and H. P. Jacobson.[6] Cooke [7] failed to obtain a positive reaction

5. Davis, D. J.: Coccidioidal Granuloma, Arch. Dermat. & Syph. **9**:577 (May) 1924.

6. Jacobson, H. P.: Coccidioidal Granuloma, Arch. Dermat. & Syph. **18**:562 (Oct.) 1928.

7. Cooke, J. V.: Immunity Tests in Coccidioidal Granuloma, Arch. Int. Med. **15**:479 (March) 1915.

in a patient when antigens were injected intradermally or drilled in with a Pirquet chisel. Jacobson [6] pointed out that Cooke's antigens consisted of cellular and intracellular products of *Coccidioides immitis* while those used by him and by ourselves consisted largely of exotoxins. Similar intradermal tests were made on the guinea-pig which had been infected with our patient's organisms. Strongly positive reactions

Fig. 10.—The absence of intra-epidermal abscesses is noticeable. The main involvement is deep in the corium. A giant cell is seen at *A*, which contained a coccidioides body.

followed in twenty-four hours (fig. 15), while the control remained negative. This confirms the work of Jacobson,[6] who obtained positive intradermal reactions in his infected guinea-pigs.

Complement Fixation Experiments with the Patient's Serum.[8]—The antigen used was a Berkefeld filtrate of a 10 day old culture of *Coccidioides immitis*

8. This work was done by Dr. Gertrude Moore of the Western Laboratories, Oakland, Calif.

grown on Sabouraud's bouillon. (It was furnished by Dr. H. P. Jacobson of Los Angeles.) The amount of the antigen used was one fifth of an anticomplementary unit. The Kolner technic was followed. A moderately positive reaction was obtained, reading + 2,200. Serums from normal patients gave negative reactions. This observation was in accord with that of David Davis,[8] who obtained complement fixation when using high concentrations of the antigen. Cooke[7] had secured negative results in his complement fixation tests. His antigens

Fig. 11.—Localization of the infiltrate around the appendages.

consisted of a saline emulsion of the powdered organisms while ours was a Berkefeld filtrate.

Precipitin Experiments.[8]—With the same antigen as was used in the preceding experiment, precipitin tests were tried on the patient's serum.

Dilution →	Undiluted Berkefeld filtrate	1 to 10	1 to 25	Other dilutions up
Results →	++	+	?	to 1:1,000 negative

This positive precipitin reaction is in accord with the observations of Cooke,[7] who obtained precipitation when using dilutions of his antigen up to 1:160.

It was impossible for us to determine the strength of our "undiluted" Berkfeld filtrate but it is certain that both it and its 1 : 10 dilution gave a positive reaction.

Roentgen Examination.—Because of discharging sinuses over both iliac bones it was felt that they were involved. A roentgenogram of the pelvis (fig. 16) showed that there was a punched-out area in the upper portion of the left ilium,

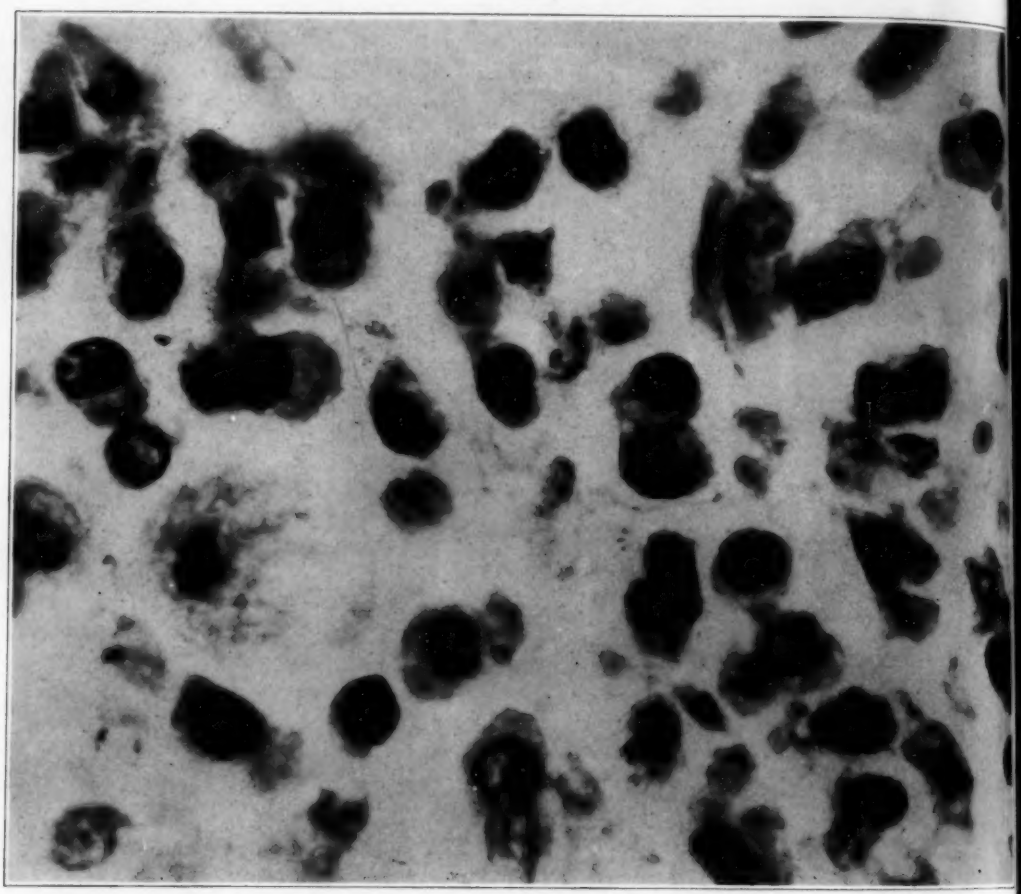

Fig. 12.—The predominance of plasma cells is seen in the infiltrate in the corium.

immediately below the middle third of the iliac crest. This area was slightly more than 1 cc. in diameter. Immediately below this there was considerable sclerosis of the bone.

There was also a necrotic area in the right ilium, at about the position of the anterosuperior spine. This process was about 2.5 cc. in extent. The lesion was on the margin of the bone, and there was a pronounced hypertrophy immediately above and below it, and also sclerotic changes adjacent to it. Roentgenologically, these lesions indicated a chronic, low-grade osteomyelitis. (The pictures and report were made by Dr. S. A. Jelte, Oakland, Calif.)

Hammack and Lacey [9] found that twenty-one of twenty-three cases of generalized coccidioidal granuloma showed involvement of the bone. There seems to be no way of differentiating the disease roentgenologically from tuberculosis of the bone. Taylor [10] suggested that when bone destruction is particularly fulminating and when a proliferative

Fig. 13.—A coccidioides body in a giant cell of the Langhans type. Endosporulation is present.

process occurs along with this destruction, the diagnosis leans toward coccidioides rather than tuberculosis. The lesions in our patient are not particularly fulminating, but the proliferative process is apparent.

9. Hammack, R. W., and Lacey, J. M.: California & West. Med. **22**:224, 1924.

10. Taylor, R. G.: Coccidioidal Granuloma, Am. J. Roentgenol. **10**:551, 1923.

Fig. 14.—Intradermal reaction twenty-four hours after the injection of Berkefeld filtrates from known cultures of coccidioides immitis. *A* and *B* show markedly positive reactions from two different antigens. Saline injected at *C* gave no reaction.

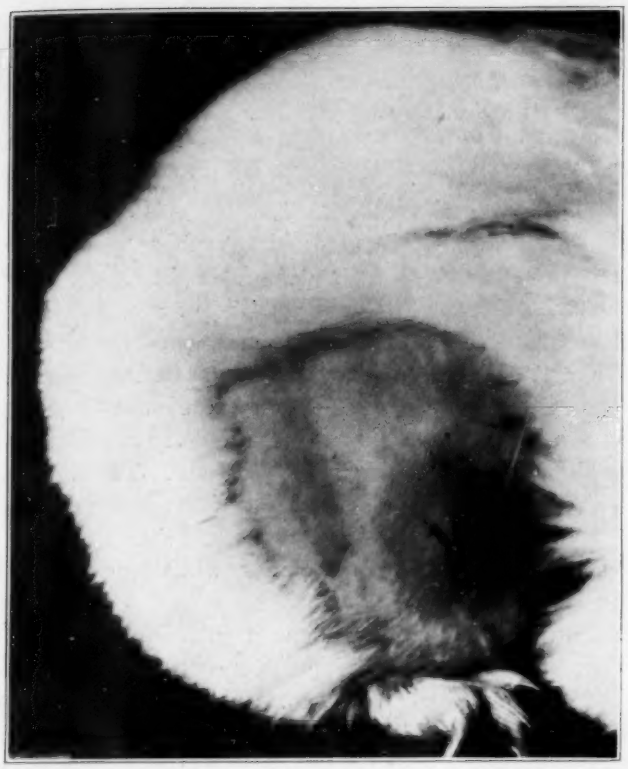

Fig. 15.—Positive intradermal reaction twenty-four hours after the injection of 0.2 cc. of a Berkefeld filtrate of coccidioides immitis. The guinea-pig was infected with organisms from the patient in case 2.

Fig. 16.—Roentgenogram of the pelvis showing destruction of the bone in the ilia. The production of bone can also be seen.

TREATMENT

The lack of response of the patient in case 2 to therapy is characteristic of all the generalized cases. In 1927, Riesman and Ahlfeldt [11] reviewed eighty-seven cases of coccidioidal granuloma and stated that no patients with generalized cases had recovered. Since then several recoveries have been reported. Guy and Jacobs [12] reported the cure of a patient after the use of antimony and potassium tartrate intravenously and the roentgen-rays locally. This case cannot be considered a generalized one, there having been no involvement of the bones, glands or lungs. Moreover, Weidman demonstrated that the organisms recovered from this case were of a low degree of virulence. Tomlinson and Bancroft [13] reported the cure and an infection of the foot (and lungs?) by the use of antimony and potassium tartrate. This patient, a medical student, evidently contracted his infection while working with *Coccidioides immitis*.

Our patient received ten intravenous injections of a 1 per cent solution of antimony and potassium tartrate in doses ranging from 1 to 10 cc. No improvement followed. Jacobson [14] reported two cases in which there was marked improvement after the intramuscular injection of colloidal copper. Our patient received ten intramuscular injections of a copper preparation, but failed to show any improvement.

Following the lead of Epstein and Miller,[15] who used foreign protein shock therapy with success in actinomycosis, we gave our patient four weekly injections of typhoid vaccine intravenously. Chills and fever ranging from 102 to 105 F. followed each injection, but no modification of the process was apparent.

Our best results followed the use of the iodides. The cutaneous and glandular lesions have improved about 75 per cent (but have not completely recovered). The osseous lesions have not been changed. The dosage was 12 Gm. of potassium iodide by mouth daily. Intravenous injections of from 10 to 20 cc. of compound solution of iodine were given twice weekly at the same time.

At present we are trying intravenous injections of gentian violet. We are doing this because it is known that a 1:250,000 dilution of this

11. Riesman, David, and Ahlfeldt, Florence: Coccidioidal Granuloma: Review of the Clinical Data with Report of a Pennsylvania Case, Am. J. M. Sc. **174**:153, 1927.

12. Guy, W. H., and Jacobs, F. M.: Granuloma Coccidioides, Arch. Dermat. & Syph. **16**:308 (Sept.) 1927.

13. Tomlinson, C. C., and Bancroft, Paul: Granuloma Coccidioides, J. A. M. A. **91**:947 (Sept. 29) 1928.

14. Jacobson, H. P.: Granuloma Coccidioides, Apparently Successfully Treated with Colloidal Copper, California & West. Med. **27**:360, 1927.

15. Epstein, N. N., and Miller, H. E.: Nonspecific Protein Therapy in Dermatology, California & West. Med. **27**:500 (Oct.) 1927.

drug will inhibit the growth of blastomyces and that it is possible to attain this concentration in the blood stream. We are aware that crystal violet has been used in coccidioides infection in rabbits and guinea-pigs [16] and that it has been of no value.

The supplemental treatment of our patient consisted of liver diet and ultraviolet light irradiations for the marked secondary anemia. After two months of such treatment the hemoglobin content increased to 75 per cent.

COMMENT

It is interesting to speculate as to the origin of the infection in case 2. The patient was raised in Mexico and had never been in the San Joaquin Valley. For a short time prior to the development of the first lesion in the cervical glands, he had worked in cotton mills which received their supply of cotton from the San Joaquin Valley. If it could be proved that the cotton was the source of his infection the case would probably come under the classification of industrial and would be compensatable.

For several years the patient went from place to place with the condition improperly diagnosed. The cutaneous lesions were labeled as syphilis and epithelioma. The glandular involvement caused a diagnosis of Hodgkin's disease to be made. Unlike most cases, a diagnosis of tuberculosis had never been made. This was because he had never shown any clinical, laboratory or roentgen evidence of pulmonary involvement. Few cases of generalized coccidioidal infection have failed to show involvement of the lungs.

For three and one-half years after infection and while he had lesions in the skin, bones and glands, this patient did heavy manual labor. This slow progress of the disease has been noted previously. In one patient nine years elapsed between the date of infection and death.[4]

It is worthy of remark that while most patients with granuloma coccidioides show involvement of the lungs, in neither of our patients were the lungs affected. The patient in case 1 showed a pulmonary tuberculosis which must probably be regarded as simple coincidence. The patient in case 2 showed no trace of injury of the lungs.

Both cases departed from the usual line of treatment, as they showed definite improvement after moderate dosage of potassium iodide.

Although it is known that many plasma cells are seen in other chronic infections, a granuloma consisting largely of plasma cells is suggestive of syphilis. The great predominance of plasma cells in our sections, amounting to almost a pure plasmoma in certain areas, demonstrates that it can occur in coccidioidal granuloma as well.

Experimental work is under way concerning the value of intravenous injections of mercurochrome-220 soluble in infected guinea-pigs.

16. Cummins, W. T., and Sanders, J.: Pathology, Bacteriology and Serology of Coccidioidal Granuloma, J. M. Research **35**:243, 1916.

ABSTRACT OF DISCUSSION

DR. ARTHUR J. MARKLEY, Denver: Colorado does not lie within the recognized endemic area of coccidioidal granuloma. Nevertheless, probably because of its relative contiguity, within the past few years a number of typical cases of this disease have been recognized and demonstrated as such. At first they were confused with sporotrichosis, and it was only the resistance of the disease to treatment that led to the correct diagnosis. Our experience with treatment has been just described by Dr. Chipman, an absolute failure of all therapeutic measures. Iodides given intravenously and by mouth have been without effect. In a number of instances, operation was resorted to, as many of the lesions were of the deep, ulcerative type, in three instances proving fatal.

As these cases were confused with sporotrichosis, it might not be without interest to call attention to the fact that Colorado lies on the western border of the recognized Mississippi Valley endemic area of sporotrichosis, but only within the last ten years has sporotrichosis been recognized in Colorado. Most of the cases have come from Nebraska and Kansas, but they are gradually creeping westward and within the last few years several cases of sporotrichosis have been seen originating in Colorado. The diagnosis can be established by microscopic and particularly by cultural procedures, and the disease is less resistant to treatment than is the one under discussion.

DR. DOUGLAS W. MONTGOMERY, San Francisco: I am glad that a cure has been found for this most intractable disease. The first case was reported, as Dr. Chipman said, by Dr. Rixford of our city and Dr. Gilchrist of Johns Hopkins, and I think that I was the next to report a case. I made a culture but thought the growth obtained was an ordinarily penicillium, which it resembles. I had no idea then that this organism had two phases of growth, a phase occurring within the tissues and another phase occurring in the atmosphere on culture medium. Dr. Rachel L. Ash, however, succeeded in cultivating the micro-organism; she injected it into guinea-pigs, and described well the life of the fungus. I think she was the first to do that work. The disease is the best mimicry of tuberculosis that I know of, both clinically and histologically.

DR. HOWARD MORROW, San Francisco: The increase in the number of patients with coccidioidal granuloma is confirmed by the fact that during the last three months we have seen three cases, all from the San Joaquin Valley. I think that more cases are seen in Los Angeles because the disease is more common in the southern part of the San Joaquin Valley and when the patients need advice they go to Los Angeles rather than to San Francisco.

It is simple to make the diagnosis if one takes a drop of pus and examines it with the high power objective on a dry field. The bodies are easily found, and one can make a diagnosis long before the culture appears in the tubes. In the San Joaquin Valley, the coccidioides have been found in the glands of some of the animals killed for beef.

Recently, a patient was seen in consultation who was a porter on a Southern Pacific train in the San Joaquin Division. He never went out of his car, but contracted the infection, which apparently was carried with dust in the wind. The organisms probably entered his body through the nasal cavities. The disease ran a rapid course, and he died within a few weeks of the time when he was first seen. The disease was not only rapid but was characterized by multiple cutaneous and subcutaneous abscesses. The fact that he came from the San Joaquin Valley made us suspicious of the diagnosis, and the examination of one drop of pus confirmed our suspicion.

DR. WILLIAM ALLEN PUSEY, Chicago: We should do all we can to relieve California of its reputation for having a corner on coccidioidal granuloma; so I refer to a case I reported in Chicago about twenty years ago.

The patient was a woman who was dying of something that closely resembled systemic blastomycosis, and finally the diagnosis was made after organisms showing endogenous sporulation were found. My patient was an immigrant from southeastern Europe, who had lived under the worst conditions but who had never been subject to any contamination from the San Joaquin Valley.

Dr. D. J. Davis of the University of Illinois has also found one or more cases in Chicago, and I believe that neither of the patients had been in the West.

DR. HARRY E. ALDERSON, San Francisco: I have had a case recently in a man from Salinas, not far from Monterey, in which the lesions were limited to the foot and lower leg, and his general condition was good. He was in Stanford University Hospital. I gave him thymol, all he could stand, and various other drugs that had been recommended, including copper, but none of this therapy had any effect except to expedite his leaving the hospital. He is now in Salinas, and his physician reports that his condition is about the same. I wonder whether some of the reports stating that patients have been cured by copper have not been premature. In a condition as serious as this, is one justified in saying that in six months or even a year a patient has been cured of coccidioidal granuloma?

DR. WILLIAM H. GUY, Pittsburgh: I have been much interested in the various types of clinical lesions that may be produced. In the one case that I reported, daily intravenous injections of antimony and potassium tartrate were used together with roentgen irradiation to all active lesions, a one-half unit dose at ten day intervals. I understand Dr. Chipman did not use roentgenotherapy when using antimony. We found that when used singly they had no effect, but when used together slow but definite improvement occurred after about one month of treatment. After two years, this man who had multiple gummatous lesions with what was diagnosed as pulmonary tuberculosis is now entirely well from the condition that was diagnosed as coccidioidal granuloma as well as the pulmonary tuberculosis.

I was interested in the results obtained from copper, in connection with Dr. Goldthwaite's statement of the effect of radiant energy on *Endameba histolytica*. Radiant energy alone had no effect on the organism, but with the addition of an infinitesimal amount of one of the heavy metals to the tubes prompt death of the amebas occurred. It seems possible that the combination of these methods of therapy, that is, the giving of one of the heavy metals and then using radiant energy, may produce results. I am at a loss to say whether the method I have outlined will be of service in other cases, because Dr. Weidman found the organism recovered from my case to be of relatively low virulence. I might say that Tomlinson's patient treated by this method remains well. I would be grateful if someone who is seeing patients with this condition would try out this combined method of treatment in some in whom other methods perhaps have failed to give results.

DR. HOWARD FOX, New York: I would not attempt to discuss this disease which is unfamiliar to me, but I understand that at this session, discussion of the cases we saw in San Francisco is in order. One of the three patients presented had a lichenoid eruption of the forehead suggesting miliary lupus. I would like to ask whether the presenter considered this eruption characteristic of coccidioidal granuloma?

DR. HIRAM E. MILLER, San Francisco: When the patient presented at the clinic on Monday was first seen, the lesions on the temples and eyebrows were not

suggestive of coccidioidal granuloma. They had been present for four years and had remained stationary and asymptomatic during that time. It was thought that the condition was a seborrheic dermatitis or something of that sort. A culture was made from the lesion at the time of his first visit, and a fungus was obtained that was thought to be a contamination. The man was lost sight of until a week ago, when he presented himself with one hair follicle pustule in the center of an area of dermatitis on the right temple. Pus taken from this lesion was found to contain double contoured organisms, many filled with endospores.

DR. H. J. TEMPLETON, Oakland, Calif.: When Dr. Montgomery said that he was glad we had a cure for this disease, I felt much as Dr. Alderson did when he spoke. We are hesitant about claiming this as a cure, in view of known relapses. This disease is classified into osseous, glandular, pulmonary and cutaneous types, but most of the generalized cases have had involvement of all of these areas. Our patient escaped the pulmonary involvement but had definite mycotic plaques on the pharynx from which *Coccidioides immitis* was isolated.

We have been guilty of using two remedies, either of which might have done some good, and we cannot tell which was responsible for the result obtained. We gave copper once intravenously, and it did no good. Whether or not the change to the intramuscular method of administering the copper produced the cure we do not know, nor can we be sure that the vaccine alone was responsible. But certainly, the combination of the two was of great value.

Answering Dr. Guy, we did use the x-rays, employing a 6 inch gap and filtering through 3½ mm. of aluminum, while using antimony and potassium tartrate, but had no result from it.

HISTOLOGIC DIFFERENCES IN A "SYRINGOMA" OF THE FACE AND SHOULDER

EMPLOYMENT OF WAX RECONSTRUCTION *

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AND
JOHN H. BESANCON, M.D.
PHILADELPHIA

Every dermatologist is familiar with the group of multiple benign epithelioma-like tumors that occur on the face and chest, and that are notorious for a diversified nomenclature. Benign cystic epithelioma, epithelioma adenoides cysticum, syringoma and other tumors are sufficient to conjure up a long series of dermatologic investigations, ranging from the time of Kaposi [1] in 1891, to that of Paul and Inglis [2] in 1927. By this time it would appear that the subject had crystallized, or nearly crystallized, at least to the extent of establishing two categories of lesions as seen histologically, and two others which might, but less certainly, be distinguished clinically. The effort has been made to correlate these two, and today there seems to be a general belief that the disease with a predilection for the chest, among other symptoms, is likely to show the histology, more or less, of the sweat apparatus (syringoma), whereas that syndrome which includes a predilection for the face is likely to show the histologic features of the epithelioma adenoides cysticum of Brooke (Howard Fox [3]). The latter is of the order of basal cell carcinoma, with extensive liquefaction necrosis of the centers of larger cell masses. It must be conceded, though, that the former (syringoma) also affects the face at times, so that there is nothing rigid about this rule; accordingly, when the disease appears on both the face and the chest it follows that the lesions, histologically, will be syringoma. This is not always the case, however, for in the case herewith reported, the lesion on the shoulder was sudorific, while the

* Submitted for publication, July 30, 1929.

* From the Laboratory of Dermatological Research, University of Pennsylvania.

* Read before the Section on Dermatology and Syphilology at the Eightieth Annual Session of the American Medical Association, Portland, Ore., July 10, 1929.

1. Kaposi and Besnier: Maladies de la peau, Paris, Masson & Cie, 1891, vol. 2, p. 365.

2. Paul, N., and Inglis, K.: Case of Epithelioma Adenoides Cysticum (Brooke), Brit. J. Dermat. **39**:195 (May) 1927.

3. Fox, Howard: Personal communication to the authors; Discussion on Syringo-Cystoma, Dermat. & Syph. **8**:138 (July) 1923.

facial ones were follicular in origin. The designation "syringoma" in our title thus is not correct in the morphologic sense; in the sense of a disease syndrome we have selected it diffidently, largely to avoid entanglements in an already replete synonymy.

The present investigation was prompted by the occurrence of lesions on one and the same patient which were apparently of both of the categories mentioned. Thus, there were numerous large lesions on the face which were fairly typical for the classic benign cystic epithelioma of that position. The second type was represented by four or five solitary lesions located on the shoulder, which were not of the type seen on the face. The lesion studied was a deep-seated, flat, homogeneous, pink papule; it projected definitely upward and did not exhibit any of the comedo-like structures such as were seen on the face. There was thus the unusual opportunity for comparing the histology of the lesions in these diverse positions on one and the same patient.

The lesion on the shoulder yielded the histologic picture of syringoma but of a highly proliferative type. The lesion from the face came from a position immediately in front of the ear. Under the microscope, the neoplastic cell nests of the latter were in some places definitely in connection with hair follicles; in others, the features of Brooke's benign cystic epithelioma were more or less remotely indicated, but certainly there was nothing syringomatous.

It is beyond the purview of this paper to speculate in detail on the significance of the foregoing circumstances, but the inference is at least permissible that the influence which was stimulating the development of the lesions on the shoulder and face was the same, and that the end-morphology was different by reason of the differing tendencies in anatomic construction in the two different regions of skin (the patient's face was hypertrichotic). It is regretted that opportunity was not also presented for examination of lesions from, say, the region of the nose, where the disease was more conspicuous, where biopsies have probably been more commonly taken in the past, and where, correspondingly, the epidermal portions of the skin may have been predominant in the histologic picture (basal cell cancer, Brooke type) rather than the sweat glands and hair follicles.

Be the foregoing as it may, it was recognized that the opportunity was at hand to study certain undetermined items of the anatomy of syringoma in the lesion on the shoulder, because many of the neoplastic cell masses could be traced into direct continuity with more or less atypical sweat ducts; the rest of this communication bears on this phase of the subject. Furthermore, it could be envisaged that these cell masses and ducts were occurring as tremendously varicose tracts winding about through the corium. It was possible for the eye and mind to follow

the intricacies of these tracts by direct examination of the sections, but this could be done only up to a certain point. In order to satisfy our curiosity as to whether such tracts communicated with the more perfectly developed sweat coils deeper in the sections, and whether any of them finally effected a communication with the surface, it was decided to resort to wax reconstruction.

REPORT OF CASE

History.—M. S., aged 39, a white woman, single, a nurse, had lesions on the face which began at the age of 13 and gradually increased until the age of 30, since which time they had been stationary. When first seen by us there were clusters of translucent nodules disposed for the most part over the middle third of the face. There were few on the cheeks, but there were particularly large clusters around the angle of the nose, on the chin and over the supra-orbital region. There were a few small ones immediately in front of the ear. Some were coalescent and exhibited slaty gray centers; none was ulcerated. The patient said that she perspired freely and that she had noticed perspiration on the lesions themselves. She also said that they itched slightly, but only in summer, and that they were more noticeable just before the menstrual period. Three sisters, who said that the lesions were more conspicuous at the menstrual period, and one brother also had the disease, as did the 6 year old son of one of the sisters. The patient's father, an uncle and an aunt were likewise afflicted.

Examination.—There were four or five lesions over the left shoulder; one, larger than the others, was different in appearance from those on the face. It was translucent, homogeneous and pink and comprised a flat, deeply infiltrated nodule. Over both shoulders there was probably a score of translucent papules, the size of a pinhead, which were somewhat difficult to distinguish from the scattered papules of acne vulgaris which were also present. There were no lesions over the chest anteriorly. Eighteen months after a biopsy had been performed on the lesion on the shoulder, a recurrence was found in the scar.

Particular attention was paid to the axillae in view of the possibility that there might be an apocrine factor in the lesions on the face similar to that in the axilla. There was profuse perspiration in the axilla, the hair was highly developed and the skin here was much more opaque and white than normally. The skin elsewhere on the body was darker than that in the axilla.

Histologic Observations.—Biopsy 1 (from shoulder): The surface of the section was uneven, apparently the result of shrinkage in fixation. The epiderm was regarded as normal in all of its layers; it was moderately thick, consisted on an average of ten or twelve layers and any epitheliomatoid hyperplasias seen deeper in the corium could not be referred to hyperplasias originating in the epiderm. There was not the slightest trace of a Krompecher effect in any of the sections examined.

The Corium: A fairly well circumscribed, but not encapsulated, accumulation of epithelial cell masses occupied the entire section except for two small portions of the corium at either end; that is, the lesion extended to the bottom of the section. All of the tumor had not been removed when the biopsy was performed. Within this general area there were at least two pilosebaceous apparatuses, each one situated at the extreme lateral margin of the epitheliomatous mass. Extending perpendicularly near its middle there was a broad strand of fibromuscular tissue which was sharply demarcated from the surrounding collagenous bundles,

Fig. 1.—Lesion from the shoulder, low power, showing general distribution of cell nests.

Fig. 2.—Lesion from the shoulder. Ductal arrangement of cells at *D*. There is a large nest of anaplastic cells extending to the right at *A*.

and which contained numerous epitheliomatoid cell nests the long dimensions of which extended parallel to this fibrous band. The suggestion was strong of some pilosebaceous or sweat gland mass which had not developed its characteristics fully but the anlage of which, including the smooth muscle, was still clearly marked. (Nipple of undeveloped heterotopic mammary nipple?)

The Tumor: The stroma consisted in part of a dense hyaloid tissue analogous to that of normal corium, but in greater part of a younger form of white fibrous tissue. In the latter, the nuclei were more numerous and of a larger size than in the collagenous portions, and the fibrils were not gathered into collagenous bundles. Disposed within this stroma there were closely packed, nicely rounded accumulations of anaplastic epithelial cells. The accumulations, while they varied somewhat

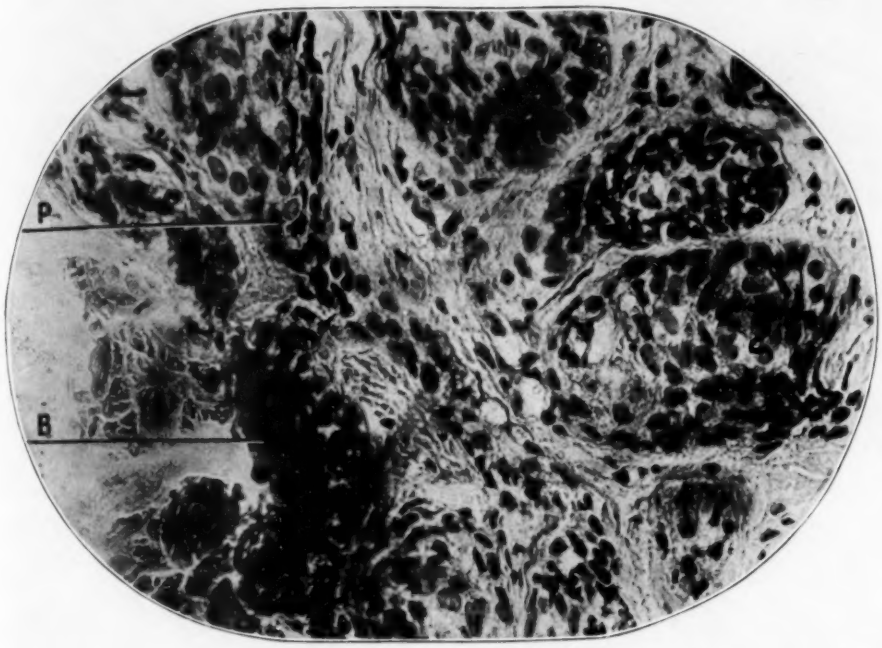

Fig. 3.—Lesion from the shoulder. Branch of ductlike cells extending downward and to the left at *B* from parent duct at *P*.

in size, were nevertheless rather uniform in this respect; they were more uniform than average carcinomatous masses. The cells within these masses varied in appearance. Thus, those in the center had markedly rarefied cytoplasms, within which either a few delicate shreds or, in rarer instances, discrete, hyaloid, greenish granules appeared. The nucleus was large, pale and vesicular. Cells in the periphery of the masses were more cuboidal, and might be likened either to those of the basal cells of the epiderm or to the lining of the sweat ducts. Sometimes they were flattened, the long dimensions of the nucleus extending parallel to the basement membrane of the accumulation.

It would be difficult to identify the precise nature of these cells were it not for features in a certain area in which the cell nests were much smaller than elsewhere and in which the stroma between them was much more abundant. This area

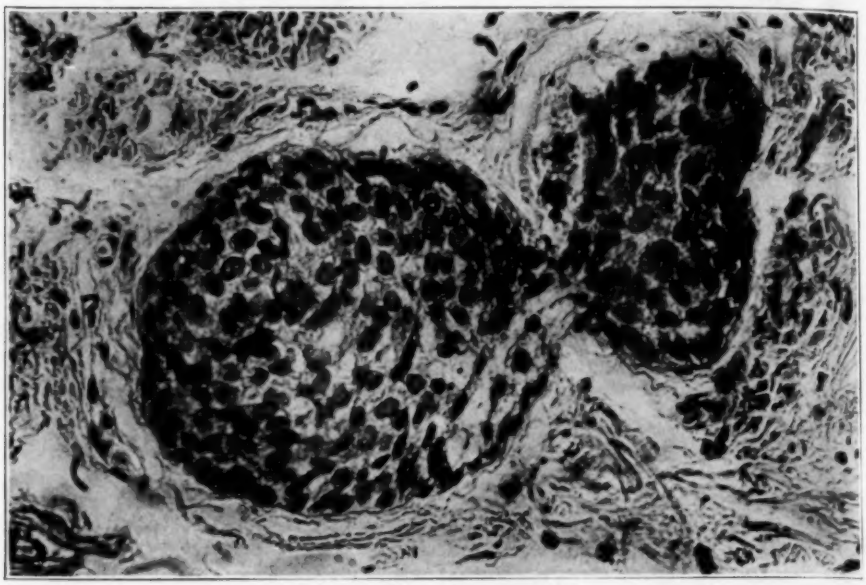

Fig. 4.—Lesion from the shoulder. Anaplastic cells with rarefied cytoplasms (secretory type). The point of fusion of two cell masses is illustrated, such as is depicted in the wax reconstruction, figures 10 and 11.

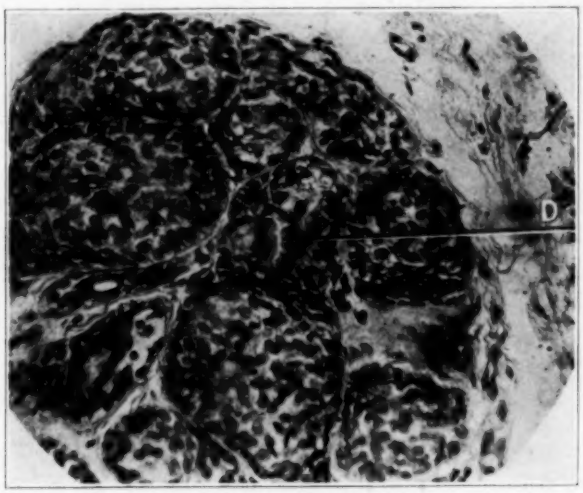

Fig. 5.—Lesion from the shoulder. Cell nests of anaplastic type. The lumen of a sweat duct is shown at *D*. Anaplastic cells are extending from the lining. The duct is clearly identified by the slitlike quality of its lumen.

occurred in the middle part of the corium near a pilosebaceous apparatus and evidently represented a position where anaplasia was less marked. In this location (where the cells were particularly highly rarefied—evidently hydropic), many were arranged more or less definitely into tubules; at least the centers of the masses were so poor in cytoplasmic substance as to suggest the development of acini. Here, too, large numbers of finer and coarser red globules more or less crowded the cytoplasm, and recalled the granules seen in the apocrine members of the axillary glands. The approach here was more to the form of the secretory than to that of the ductal portions of the sweat glands. Around most of the cell nests

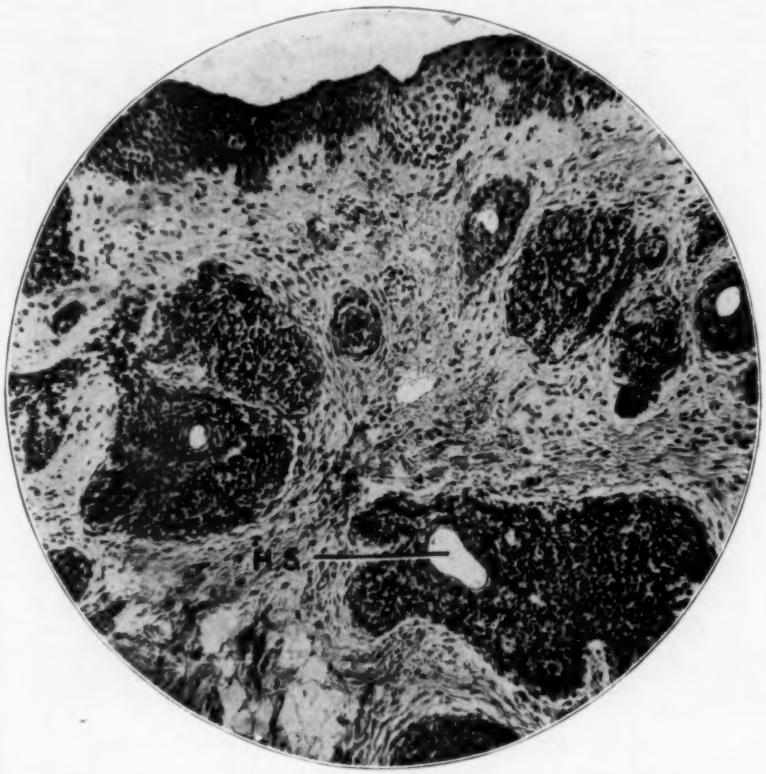

Fig. 6.—Lesion on the face. Basal cell in type, contrasting with syringoma features in the lesion from the shoulder. See figure 7 for details of the hair space at *H. S.*

a narrower or broader mantle of hyaline fibrous tissue was thrown, which resembled involuntary muscle in its arrangement, but which was otherwise identical with the collagen strands of the stroma.

A further circumstance that swung us to the opinion that these structures were of sudoriferous rather than hair follicle or basal cell origin was the fact that eventually a long, continuous, double row of cells was discovered in some of the cell masses in the most superficial part of the fibrous and epitheliomatous column, which was referred to at the beginning of this description. This could mean only

that the duct of a sweat gland and its direct extension downward into this definitely restricted area indicated that the cell islands here were alined to the sweat apparatus rather than to any other.

A few properly formed sweat glands were included in the deepest parts of this section, but all of these lay at the margins, apart from the central tumor mass. They served admirably as controls, and were of eccrine type. Also, a number of normal appearing sweat ducts could be identified, insinuating themselves between the anaplastic cell nests. Portions of two or three sebaceous glands were also included; one of these appeared normal. The second, the larger, showed extensive degeneration of its cells, which had become rarefied, fibrillar and more or less

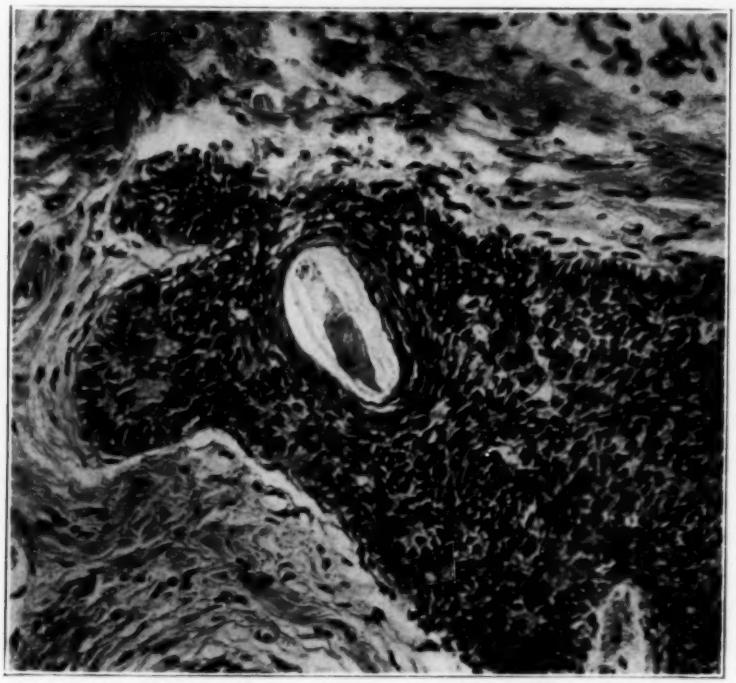

Fig. 7.—Lesion from the face. Basal cell characteristics in the cell mass, and presence of an abortive hair. Suggestion of origin of the process in a hair follicle.

fused. A few polymorphonuclears and some hyaloid bodies of irregular size were also present; the identity of the latter could not be established.

Biopsy 2 (from face): The patient had received four or five applications of roentgen rays between the time of the first and the second biopses. The second specimen was removed from a position immediately anterior to the left ear, where there were a few small, deep-seated nodules.

Microscopic Examination.—The Epiderm: The surface of the skin was comparatively even. The stratum corneum was thin, and, while the stratum granulosum and prickle cell layers were thin, they were definitely indicated. There was nothing abnormal in the least respect in the basal cells. On the whole, the epiderm was of an extremely thin type, averaging in all not more than eight or ten layers in any part.

The Corium: The papillae in the corium were small, but otherwise appeared normal. Nothing abnormal could be made out about the blood vessels. The important feature of the section consisted in the presence of goodly numbers of cell islands which extended from the subpapillary region to the subcutaneous fat. Some of the islands were small, others were large, and many were more or less confluent. They were of all shapes, some being practically circular and others extremely irregular; there were numerous examples in which a circular form showed shorter or longer buds extending from the periphery. This reminded one strongly of the tasselated appearance which is often normally seen at the junction of the sebaceous gland with the hair follicle. The cells concerned were of a small, more or less spindle type, the ones in the periphery of the islands being particularly so, and showing their long dimensions perpendicular to the basement membrane. The cells in the interior of the areas had their long dimensions arranged irregularly.

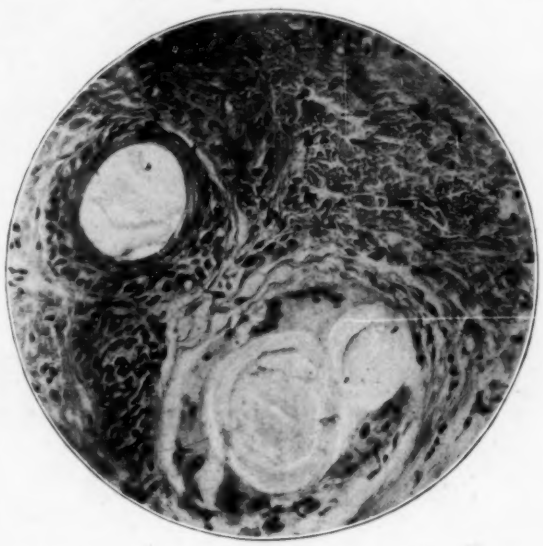

Fig. 8.—Lesion from the face. Foreign-body granuloma, enclosing degenerate keratinous material.

The most engaging features of the section, apart from the fact that we were dealing with a carcinoma which was obviously in the category of the basal cell, was the presence of smaller and larger cystic spaces within the islands. Some of the spaces were irregular and showed no definite lining. In others, however, the lining was definite. The cells comprising it appeared compressed, and the lumen was broad as though there had been dilatation of some preexisting space. The appearance was thus good for distended sweat ducts; but, in the light of data which will be submitted later, this is open to question. There were other spaces which were exceedingly small and which were bordered by cells which had the general appearance of those which one meets where the sweat ducts pass through the epiderm; that is, one did not see two definite layers of cuboidal cells, but the cells were slightly larger and paler and, furthermore, occasionally contained a few eleidin granules. In these respects they differed from other cells of the epiderm and of these islands. Then, again, some of these spaces were much larger than

others and contained keratinous material, sometimes of a delicate pale pink-staining quality but at others a heavy, lumpy, intensely red-staining. In many of these instances the material was arranged in circumferential lamellae which simulated pearly bodies but fell far short of being the genuine article.

There were thus some appearances in these spaces which could aline them to the hair follicle and others to the sweat glands; in no case were we able to identify a hair shaft in any of them; yet such spaces, except for the actual presence of a

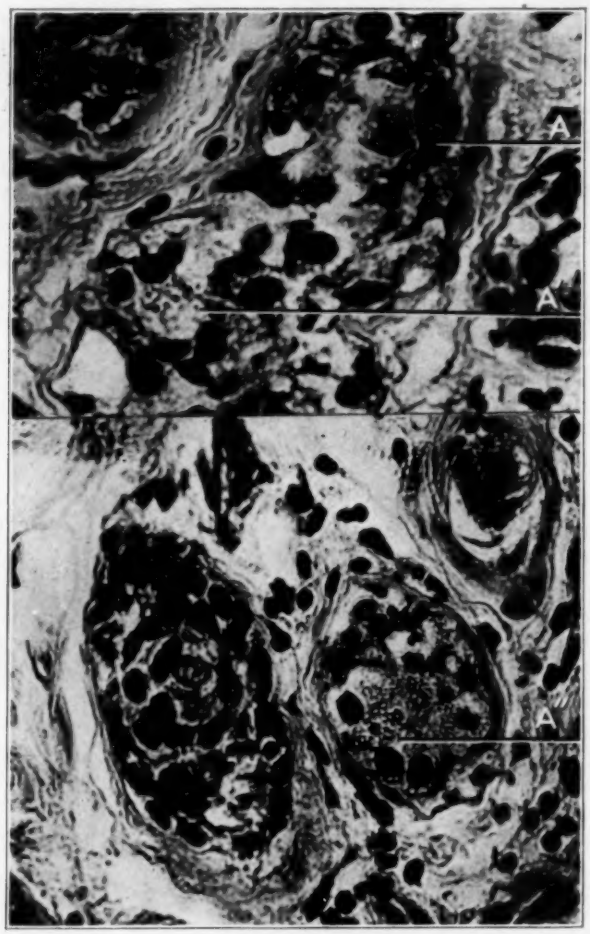

Fig. 9.—Sweat cells of apocrine type at *A*, *A'* and *A"*. The spherules in their rarefied cytoplasms were brilliantly red and refractile. The granules in *A* were so closely packed that the cytoplasm appeared almost solidly red.

hair shaft, were in many cases identical with those in the epiderm proper, in which the hair shafts were still present. The fact, too, that the hair shafts in some of the normal follicular orifices of the epiderm were wrinkled, distorted and evidently never developed perfectly, tends to confirm the impression that many of the abnormal spaces in the cell islands deeper down were of hair follicle nature, although the complicating effects of roentgen therapy must be kept in mind.

The key to the situation was furnished by the hair follicles at the very margin of the lesion. There were hypoplastic and were comprised of cells comparable to those already described as being arranged in nests or masses; such cells were elongated and of the type commonly seen in Krompecher carcinoma. They were alined with the pilosebaceous apparatus; this piece of evidence was unequivocal in identifying them. A hair shaft could be discovered in only one or two instances; generally, there was but an accumulation of keratinous material where the shaft should be.

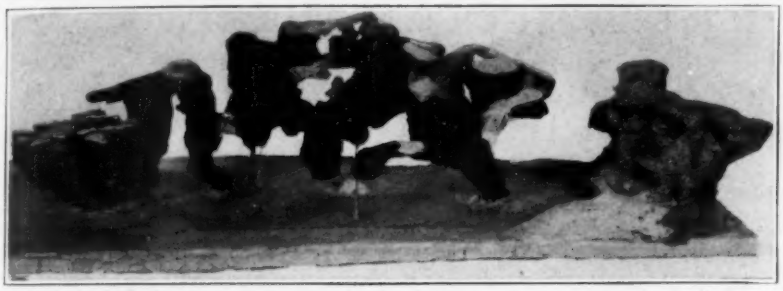

Fig. 10.—Wax reconstruction of a portion of the lesion. The detached mass at the right represents the epiderm; the confused mass at the left, syringoma tubules.

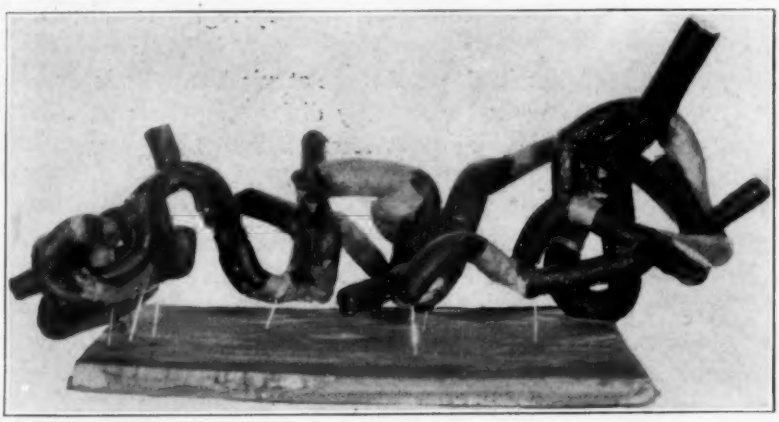

Fig. 11.—Adaptation from the reconstruction, bringing out more clearly, among other things, the anastomoses between the tubules. The pale parts were comprised of more undifferentiated types of cells; the darker of anaplastic cells.

A solitary group of sweat coils was found deep in the corium. Immediately above it there was a hugely dilated sweat duct. It was not possible to trace a duct from this gland to the surface.

Foreign-Body Granulomas: There were several foreign-body granulomas scattered through different parts of the section, more particularly in the deeper regions. They consisted almost exclusively of small foreign-body giant cells with rather abundant cytoplasms and with indefinite outlines. Few lymphocytes were asso-

ciated with these granulomas. The interior of some of them (the granulomas) contained clumps of keratinous material.

RECONSTRUCTION METHODS

Nine hundred and seventy-six sections of the lesion from the shoulder were cut in paraffin at 6 microns. The portions selected for reconstruction extended through a position where the ramifications of the tracts were less intricate and where the transitions from ducts to anaplastic cells were best defined. Sixty-five sections were utilized for reconstruction, the images being projected on paper and drawn in outline. Wax plates were cut out from these patterns and superimposed and arranged according to the classic technic of Born.[4] It is understood, of course, that this work was checked up during its progress by direct observation and comparisons of the sections themselves under the microscope.

ANALYSIS OF RECONSTRUCTION

The considerations herewith in connection with the reconstruction are in terms of the sweat glands exclusively, as the histologic sections did not reveal any evidence that other structures were concerned or related to the abnormal sweat structures. The sweat tubes were found to coil intricately both high and low in the corium, and comprised varicose tracts extending from the subpapillary region to subcutaneous tissue.

The first point determined was that the atypical, neoplastic structures did not communicate with the perfectly differentiated sweat glands in the deepest parts of the section, at least so far as the reconstruction went. We are satisfied, however, from following through sections by microscopic observation direct, that this also holds good for the neoplastic portions at other levels than that of the reconstruction.

The second point determined was that there were no isolated cell nests; that is, none of the anaplastic cells had become detached, either as individuals or as groups, from the parent sweat apparatus and passed to an independent isolated position. Or, in other words, there was no permeation of tissue in the sense of a true disjunctive malignant metastasis.

The greatest surprise of the entire work came in the discovery that the tracts were branched. There were about twenty branches in the comparatively small bit of tissue represented in the reconstruction. They were irregular in form and at times consisted of duct cells and in others of the completely anaplastic cells.

Anastomoses between the tracts were frequent. They occurred, again, in most irregular fashion; they consisted of duct or of anaplastic

4. Born, G.: Die Plattenmodellirmethode, Arch. f. mikr. Anat. **22**:584, 1883.

cells or of both; at times they consisted simply of fusions of adjacent groups of tracts and at other times comprised more or less elongated bridges between distant coils.

One of the points that was raised in an introductory paragraph of this paper was whether the tracts communicated with the surface; this remains unsolved by a study of the reconstruction. So far as the reconstruction went, there were no communications, but this, of course, is not final. Thus, it was possible to single out tracts which ended blindly (confirmed by direct examination of sections) and to imagine that such could be the uppermost terminus of the entire complex. With the appearance of side branches, however, which extended beyond the limits of the reconstructions, it becomes impossible to deny that any one of these side branches might also be such a terminus.

It is significant, however, that all of the ducts which were observed to discharge on the surface (976 sections examined) were of normal construction and probably terminated in the normal coil glands deep in the corium. None of them included or were continuous with anaplastic cells, from which it is reasonable to infer that the syringomatous tissue did not communicate with the surface. We cannot go further on account of the winding propensities of sweat ducts which prevent, in sections, a final decision that they did not connect at some deeper level.

In view of the extreme complexity and intercommunication of these tracts, involving such numerous side branches, it is clear that a comparatively small number of sweat units would suffice to yield a grossly visible "tumor." Indeed, there were no less than sixteen positions in the reconstruction in which side branches were found to be continuing outward to unknown distances, and in which the continuations could not be included in the reconstruction on account of practical limitations in the size of the reconstruction; theoretically, it would be necessary for the etiologic embryologic vice to affect but one sweat anlage in order for it to be represented by a grossly recognizable lesion.

SUMMARY AND COMMENTS

Heretofore, as far as we can find, the multiple benign epithelioma-like new growths with predilection for the chest have shown the histology of sweat apparatus, whereas those of the face were likely to show, more or less, the features of epithelioma adenoides cysticum of Brooke. It now appears that lesions in one and the same patient may be of both the categories mentioned. Perhaps if multiple biopsies had been taken from both places in cases previously described in the literature, both derivations would also have been demonstrated. In the lesion on the shoulder there was no metaplasia of sweat apparatus morphology into that of the pilosebaceous or epidermal, but in the

lesion on the face, while not evident, metaplasia could not be so positively excluded.

Relating the observations in the reconstruction to those of the histologic sections, it becomes clear that in this material all of the elements in the lesions on the shoulder should be regarded as sweat apparatus genetically.

Some cells contained coarse refractile red granules similar to those found in the apocrine glands of the axilla; this appears to be the first time such an observation has been recorded in syringoma. It conspires to give additional apocrine flavor to the history of syringoma.

From the reconstruction, one learns that (1) this tumor consisted of tracts of cells coiling from the subepidermal levels to the subcutaneous tissue; (2) the neoplastic structures did not communicate with perfectly differentiated sweat glands; (3) none of the cell nests was isolated; that is, there was no permeation of tissue in a metastatic sense; (4) the tracts of cells were branched, anastomosed frequently, were irregular in form and consisted in some places of duct cells and in others of completely anaplastic ones; (5) apparently none of the tracts communicated with the surface, and (6) a small number of sweat units would suffice to yield a large sized tumor—apparently a solitary sweat anlage could result in a grossly recognizable lesion.

In view of such disorder of the anatomy as the syringoma reconstruction shows, together with other data that have been recorded already, we believe that this particular lesion extends beyond the concept of simple nevi; it is a neoplasm. While we dislike to insert another item to the already overburdened synonymy, we feel that this is a true sweat gland adenoma.

The histologic sections are deposited as follows: Army Medical Museum, Washington, D. C., Accession no. 30888, and Laboratory of Dermatological Research, University of Pennsylvania, Philadelphia, Accession no. 1563. The wax reconstructions are also at the latter place.

ABSTRACT OF DISCUSSION

Dr. Howard Fox, New York: The essayists are to be congratulated on their painstaking study by innumerable serial sections and wax reconstruction of a disease that has caused much discussion. As they stated, the lesions occurring on the face usually show the histologic changes of the benign cystic epithelioma type, while those on the trunk are of the syringoma type, the former being apparently related to the follicles and the latter to the sweat ducts. The writers were fortunate in being able to study both conditions in the same patient.

A new observation of interest was the presence in the syringoma lesion of granular bodies suggesting a relationship to the apocrine glands of the axilla. I was particularly interested in the conclusion that the syringoma lesion on the shoulder was a neoplasm and not a nevus. This might explain the fact that such lesions may disappear after treatment with the roentgen rays. In a case of this kind in a negress, I treated one side of the trunk experimentally with a dozen

fractional doses of unfiltered roentgen rays. This was followed by complete involution of the lesions which were irradiated.

DR. WEIDMAN, Philadelphia: While we all know that this disease is familial (such has been repeatedly reported), little opportunity has been given to inquire into details, genetically speaking. But fortunately for us, this young woman was a member of a prolific family, and I was able to chart out almost thirty members in three generations, and among these six or seven had the disease. The outcome of the analysis was that it was not transmitted through either males or females alone, but through both.

In reference to Dr. Fox's point; with the lesion on the shoulder I could see how it was originally nevic in nature, but it had exceeded in activity all the ordinary nevoid structures; it was neoplastic. That would still leave a hyperplastic property in the cells, endowing them with such a property, as Dr. Fox said, that they would be more amenable to roentgen irradiation than those of the ordinary nevus.

Obituary

LUIGI PHILIPPSON, M.D.
1862—1929

Luigi Philippson, professor of dermatology and syphilis at the University of Palermo, Sicily, a corresponding member of the American Dermatological Association, died suddenly at his home on Nov. 24, 1929, at the age of 67.

Philippson was born in Lubec, Germany. He obtained his medical degree at Leipzig in 1887, and for several years was assistant at Unna's Dermatological Institute at Hamburg, where he laid the foundation for the thorough knowledge of dermatopathology which all his writings exhibited.

In 1893, Philippson joined Professor Tommasoli, head of the Palermo Clinic, as his first assistant, and, on the death of Tommasoli in 1905, succeeded to the professorial chair.

He was deeply interested in the treatment and prevention of lupus, one of the outstanding problems of Sicily and Southern Italy, and his work received the recognition of a gold medal at the Hygienic Exposition in Rome in 1911. During the World War he proved a loyal son of his adopted country and served as a colonel in the Medical Corps.

Philippson was a retiring, modest man of wide culture, with a rare kindliness of heart. In Palermo he was called "the father of the poor." He is survived by his widow and two sons.

S. P.

Correspondence

TREATMENT FOR EPIDERMOPHYTOSIS

To the Editor.—The great number of applications advised in the treatment for epidermophytosis proves that none can be depended on for uniform good results. About five years ago I started to experiment with an ointment consisting of the following: sulphur precipitate, drachm 1; salicylic acid, drachm ½ and zinc paste, ounce 1. The paste is relied on for drying, the salicylic acid for exfoliative and the sulphur for parasiticide effects. The diseased patches are vigorously scrubbed with soap once daily and the ointment rubbed in thoroughly twice daily. I was surprised at the consistent good and quick results of this method, and I have used it exclusively ever since. Dr. R. L. Sutton who tried it also praises it highly. I should be glad to hear the experience of others.

ALFRED SCHALEK, M.D., Omaha.

CORRECTION

In our recent article on "Dermatosis Papulosa Nigra" (ARCH. DERMAT. & SYPH. **20**:629 [Nov.] 1929), we called attention on two occasions (pp. 633 and 637) to the similarity of the histologic picture of senile keratosis and dermatosis papulosa nigra. This was a mistake. We really meant verruca senilis instead of keratoma senile as we have recognized the distinction between these disorders since the article of Freudenthal (*Arch. f. Dermat. u. Syph.* **152**:505, 1926). Old teaching did not clearly distinguish between keratoma senile and verruca senilis, but we believe that we should do so now.

J. C. MICHAEL.
E. R. SEALE.

Biography

LAURENT THÉODORE BIETT

B. BARKER BEESON, M.D.
CHICAGO

Laurent Théodore Biett, a Swiss, was born at Schampf, in the Canton of Grisons, in 1781. Seven years later his parents fell heir to a house in Clermont-Ferrand, which necessitated their removal to France. Biett was at first a student in the Central School and College of Clermont. He began the study of medicine in that same city at the Hôtel Dieu. His teacher was Bonnet, a prominent local surgeon and a pupil of Desault, whom many have acclaimed as the leading surgeon of his day. Biett soon showed considerable proficiency as a student. After exhausting the medical resources of Clermont-Ferrand, he went to Paris to complete his medical education. Biett matriculated in the École Pratique and even competed for a prize but lost to Breschet, who later became a professor in the Paris Medical Faculty. Being very poor, he was compelled to write articles for the Dictionary of the Medical Sciences. Later, he became its director. Soon after reaching Paris, Biett became acquainted with Alibert, who at once took a fancy to the serious, hardworking young Swiss and soon secured his collaboration in some of his writings. Biett wrote the chapter on mineral waters for Alibert's "Elements of Therapeutics" (1813). The author even dedicated that work to him in these flattering terms: "To my most beloved pupil, L. Biett, a young man of great promise, who, although he has already accomplished much, is continually endeavoring to advance farther and is ever urged to greater things. On many occasions I have conversed most delightfully and with great practical benefit, with him, concerning the healing of disease."

In 1813, Biett was admitted to the Saint Louis Hospital, where he aided in caring for the wounded and the patients with typhoid from one of the Napoleonic campaigns. Twenty years later, he again took an active part in similar work. An intensive study of five cases observed at Saint Louis formed the basis of his thesis entitled "Acute Idiopathic Frenzy," which was submitted in 1814. That same year a dispensary for outpatients was opened there, and Biett was placed in charge, owing to the influence of Alibert. He kept this position for twelve years. In 1820, Biett was made an adjunct physician to the Hospital Saint Louis, and in 1825, he was named attending physician to that same institution. This last appointment is said to have been due in a large

measure to his close relations with the members of the general hospital board, on whom his untiring zeal had made a deep impression. Earlier they had even made him a sort of inspector of the Parisian hospitals and had asked his advice as to their betterment.

In 1816, an event occurred which profoundly affected Biett's career. He was asked to accompany, in a medical capacity, a young man who belonged to a wealthy and influential French family, who was desirous of foreign travel. Biett and his patient visited Italy, Switzerland and

LAURENT THÉODORE BIETT, M.D.
1781-1840

England. While in London, he attended the clinics of Bateman at the Public Dispensary and was thus introduced to the Willanistic doctrine. On being appointed a full-fledged physician to the Saint Louis Hospital, Biett selected that classification as a guide in his teaching and hospital work. He did not accept it entirely but with certain reservations. Brodier, in his splendid work on Alibert, stated that Biett attempted to persuade Alibert that his own classification was far from perfect, and also that Willan's was not really opposed to it but was rather different and embodied certain features which Alibert could

profitably incorporate into his own. Alibert apparently did not relish these suggestions, so he gradually became estranged from his pupil. By 1826, there were two schools of dermatology in the celebrated old hospital. Biett was most careful to praise his teacher at every opportunity, but certain of his followers were less diplomatic and prone to ridicule the ideas of the author of the "Arbre des dermatoses," which served only to widen the gulf between Alibert and Biett.

The contrast between Alibert and his outstanding pupil was a striking one. Hardy, in a most interesting letter to Besnier, said that one went to Alibert's clinics under the trees and close to the Pavillon Gabrielle in order to be amused, while one visited Biett's wards in the Pavillon of Saint Matthew in order to learn. Alibert delighted in metaphors and similes, which, although highly diverting, were of little teaching value. Biett was clear, concise and eminently practical. He was not an orator like Alibert, but on certain occasions appeared to be even bashful and was always more or less retiring. While the character of Biett was apparently not so forceful as that of Alibert, yet it was of sufficient strength to enable him to realize a very considerable progress in French dermatology. Brocq considered him as the real founder of the French school. Biett's grave demeanor contrasted most strikingly with the vivacity of Alibert. He has even been termed a poseur by some. Biett was kind and at times even devoted to his pupils and patients, but his natural reserve always held them at a certain distance. He was tall and robust. A high forehead and well developed cranial vault marked him as a thinker and a deep student, capable of penetrating into the innermost depths of a given problem. Biett's countenance was kindly and agreeable. Sagacity, calmness and depth were expressed in his glance.

Early in his medical career, Biett became acquainted with a number of prominent Parisian families, mostly Calvinists like himself, and they aided him considerably. It was not long before he was numbered among the more prominent physicians, not only of Paris but of France. Being well versed in general medicine, as well as in dermatology, he was much in demand and was even called to distant points in Europe. Count Molé, who was very influential during the reign of Louis Philippe, was his close friend, and he doubtless facilitated Biett's entrance into the higher circles. Being very fond of the arts, Biett was the personal physician of a number of the better known painters and sculptors, and many members of the theatrical profession likewise availed themselves of his skill.

Biett was an excellent teacher, his lectures being both interesting and thorough. He stressed the importance of both diagnosis and treatment at a time when the latter was much neglected. Aside from articles

for medical journals and dictionaries, he wrote but little. His lectures were published by Cazenave and Schedel. Biett performed the autopsy on Talma, the celebrated tragedian, and reported his results before the Academy of Medicine. He is generally credited with being the first to describe accurately the syphilids, and in its main points, his description still holds good. Biett also described the collarette of adherent scales which is frequently found about the bases of syphilitic papules. While not pathognomonic, he believed that it was valuable in the differentiation between syphilis and psoriasis. Biett described lupus erythematodes under the title of "Erythème centrifuge." In autopsies on cases of pemphigus, he noted the frequency of fatty degeneration of the liver.

Biett was much interested in therapeutics at a time when most dermatologic energy was being devoted to classification. He gave sulphur, arsenic and iron internally. He is credited with the formula for the Asiatic pill. Hardy has stated that Biett was partial to the giving of arsenic in the chronic skin diseases and to the use of the alkalis in some lichens. His favorite remedies in syphilis were the protiodide of mercury and the biniodide of mercury. He employed hydrotherapy extensively, especially in the form of sulphur baths. He installed apparatus at Saint Louis whereby dry air and hot air could be used in treating skin diseases. Like Paré, he employed vesicants and caustics. Bleeding and the free use of purgatives were also included in his armamentarium. As a therapeutist, we are told that he was daring but so skilful that he was able to avoid bad results.

In addition to being a charter member of the Academy of Medicine, he was an officer of the Legion of Honor. Cazenave, Schedel, Gibert and Behier were his chief pupils. Brocq believed that he influenced Devergie and even Bazin.

Biett died of an aortic disease in 1840, at the age of 59. He deserves to rank among the best known members of that school with the founding of which he had so much to do.

Abstracts from Current Literature

THE OCCURRENCE OF POSITIVE WASSERMANN REACTIONS IN THE SPINAL FLUID OF TUBERCULOUS AND OTHER NONSYPHILITIC CASES OF MENINGITIS. K. SCHAFFLE and M. RIESENBERG, Am. J. M. Sc. **178**:632 (Nov.) 1929.

Positive Wassermann reactions in spinal fluids from nonsyphilitic patients could possibly be explained, according to the writers, by the abundance in the system of micro-organisms causing the inflammation.

The Wassermann test on the blood was negative in the cases reported, the gold curve being of the meningitic type significant of a process other than syphilis.

JAMIESON, Detroit.

GLANDERS. RALPH W. MENDELSON, J. A. M. A. **93**:1379 (Nov. 2) 1929.

Two cases are reported, in which *Bacillus mallei* was isolated from skin lesions on the nose and the upper lip. Both patients had been in contact with horses that died of unknown causes some months previously. Following a purulent nasal discharge there appeared small vesicles near the tip of the nose. These slowly developed in an impetiginous manner until the nose and the upper lip presented a moist ulcerated surface covered with heavy yellow crusts. In one patient the initial lesion was in the right eye. There were no systemic symptoms. Treatment with autogenous vaccines was satisfactory.

MIDLINE PRESTERNAL ULCER FREQUENTLY A GUMMA. OWEN H. WANGENSTEEN, J. A. M. A. **93**:1380 (Nov. 2) 1929.

In the absence of cardinal signs of syphilis, the presence of a midline ulcer should arouse a suspicion of syphilis, for syphilitic ulcers are apt to choose the midline where the blood supply is normally the least. A case in point is cited, in which a shallow ulcer developed over the sternum, with little change in the adjacent skin. The Wassermann reaction of the blood was negative and there were no other manifestations of syphilis. The lesion healed after treatment with arsenic and iodides; subsequently there developed a typical syphilitic perforation of the nasal septum.

TRUTHS ABOUT THE SERUM DIAGNOSIS OF SYPHILIS WITH ESPECIAL REFERENCE TO THE KOLMER AND KAHN REACTIONS. JOHN A. KOLMER, J. A. M. A. **93**: 1429 (Nov. 9) 1929.

A study of the literature on the subject of serology in syphilis reveals so many conflicting reports that the author thought it would be useful at this time to list what he terms as truths about the serum diagnosis of syphilis. The fact that the serologic reactions still hold high rank after withstanding the vicissitudes over a period of twenty-five years shows that they are of real and of intrinsic value. The various tests, though biologically nonspecific, possess a high degree of practical specificy, and the false positive reactions that occur are almost entirely due to technical errors. The tests are indispensable aids in diagnosis, and are sometimes the sole means of detecting syphilis in concealed stages. For this reason, two or more procedures as complement fixation and precipitation tests should be employed —and more widely used as routine measures in the practice of medicine. It is the author's opinion that the various serum tests are not too sensitive, and they are of valuable aid in guiding the treatment of syphilis and as criteria of cure. Spinal fluid examinations are now recognized as an important part in the diagnosis of syphilis. The article is essentially a critical review of the literature.

THE TREATMENT OF SYPHILIS IN ITS RELATION TO PREVENTION. THOMAS PARRAN, JR., J. A. M. A. **93**:1793 (Dec. 7) 1929.

Parran notes that since the World War there has been a remarkable decrease in the number of cases of early syphilis in European countries, notably in the Scandinavian countries, Germany, Belgium, England and to a lesser extent in France. This is attributed in every instance to the application of early and energetic treatment, for it is on this one point that administrative and educational activities have been centered. Although accurate data as to the trend of new syphilitic infections in this country are lacking, it does not appear that the venereal disease control campaign has produced in the United States results comparable with those which have been reported from Europe. This may be due to the fact that in the United States about half of all patients with syphilis are treated privately, whereas in the European countries most patients are treated in clinics responsible to the governments. In the United States the family physician is first called on to treat the patient for syphilis; and the family physicians have not been studying the problems from the point of view of prevention. It is the duty of the health officer, the medical society and the medical schools to see that this condition is corrected.

RATTNER, Chicago.

ETIOLOGY OF OROYA FEVER. XVI. VERRUGA IN THE DOG AND THE DONKEY. H. NOGUCHI, H. R. MULLER, E. B. TILDEN and J. R. TYLER, J. Exper. Med. **50**:455 (Oct.) 1929.

Inoculation of a dog with *Bartonella bacilliformis* resulted in local reaction only; definite verruga lesions, however, were produced.

Intravenous inoculation in donkeys was followed by large soft swellings which did not resemble verruga.

DEVELOPMENT IN TISSUE CULTURES OF THE INTRACELLULAR CHANGES CHARACTERISTIC OF VACCINAL AND HERPETIC INFECTIONS. T. M. RIVERS, E. HAAGEN and R. S. MUCKENFUSS, J. Exper. Med. **50**:665 (Nov.) 1929.

Rabbit corneas infected and cultivated in vitro developed characteristic vaccinal and herpetic lesions, including Guarnieri bodies and acidophilic nuclear inclusions.

A STUDY OF VACCINAL IMMUNITY IN TISSUE CULTURES. T. M. RIVERS, E. HAAGEN and R. S. MUCKENFUSS, J. Exper. Med. **50**:673 (Nov.) 1929.

Typical vaccinal lesions, associated with Guarnieri bodies, developed in normal corneas inoculated with vaccine virus in vitro and cultivated in antivaccinal plasma.

Immune corneas developed either mild vaccinal lesions or none at all.

JAMIESON, Detroit.

A STUDY OF THE PELLAGRA-PREVENTIVE ACTION OF CANNED SALMON. JOSEPH GOLDBERGER and G. A. WHEELER, Pub. Health Rep. **44**:2769 (Nov. 15) 1929.

The study revealed that canned salmon (Alaska chum) contains the pellagra-preventive factor. Because of its availability in the preserved state, salmon may be considered a fair substitute for meat in the regions where pellagra is endemic when meat is not readily available.

RATTNER, Chicago.

THE ETIOLOGY OF ALOPECIA AREATA AND ITS RELATIONSHIP TO VITILIGO AND POSSIBLY SCLERODERMA. W. H. BROWN, Brit. J. Dermat. **41**:299 (Aug.-Sept.) 1929.

Brown discusses the subject of alopecia areata in detail on the basis of a survey made in three hundred cases. He states that one cannot completely separate the areate forms from the diffuse variety, as both may be a manifestation of the

same etiologic factor. He discusses the subject under the following headings: age incidence; sex incidence; color incidence; incidence of nervous symptoms; hereditary incidence; position and number of patches; course; etiology; the trophoneurotic theory, with brief records of four cases of alopecia following mental strain; alopecia following traumatism; evidences of involvement of the sympathetic nervous system; what is the evidence in relation to alopecia areata?—with numerous references to the literature; epinephrine blood sugar reaction in alopecia; observations on the blood sugar; focal sepsis; alopecia and syphilis, and alopecia and its possible relation to vitiligo. He concludes from a consideration of the subject under these headings that no one etiologic factor will explain all cases of alopecia, but that it is a clinical entity which may be caused by various factors acting singly or in combination, and that there is strong evidence to support the theory that the following factors play an important rôle in its causation: (1) psychic or mental stresses and strains of all kinds arising from anxiety, emotion, fear, overwork, etc.; all act by transmitting abnormal impulses through the sympathetic or endocrine-sympathetic system to the hair papillae, disturbing the factors concerned in its nutrition; (2) physical trauma which seems to act in the same way; (3) focal sepsis of all kinds, but more especially infection of the tonsils, teeth, nasopharynx, maxillary antrums, frontal sinuses; much less frequently from intestinal causes; (4) disturbances of the endocrine and vegetative nervous system; (5) constitutional emotional instability, which is a prominent predisposing factor, and (6) age, sex and family predisposition, which are also important factors exerting an influence on the origin of alopecia areata.

INFLUENCE OF THE MIND ON THE SKIN. BONJOUR, Brit. J. Dermat. **41**:324 (Aug.-Sept.) 1929.

Bonjour refers to the work of Sack in the November, 1928, issue of the *British Journal of Dermatology and Syphilis* and refers to his prior work and that of other authors on this subject. He discusses briefly the value of psychotherapy in the treatment for warts, eczema, erythroderma, hyperhidrosis, urticaria, hay-fever and asthma. He feels that patients suffering with the skin diseases mentioned are persons whose nervous system is affected either through an emotion or through some other cause of excitement.

THE ETIOLOGY OF ALOPECIA AREATA AND ITS RELATION TO VITILIGO AND SCLERODERMA. A. C. ROXBURGH, Brit. J. Dermat. **41**:351 (Oct.) 1929.

Roxburgh briefly enumerates the various principal theories that have been put forward to account for alopecia areata, and states that the theory which seems to be supported by most modern authorities is that alopecia areata is caused by some defect or alteration in the secretion of one or several of the ductless glands associated with a disturbance of the sympathetic nervous system. Similar vague causes are regarded as being responsible also for vitiligo and scleroderma. In forty-two cases of alopecia areata, coexisting vitiligo was found in only two. One feature found in common in alopecia areata, vitiligo and scleroderma is that all three usually occur in isolated patches the distribution of which cannot be brought into line with that of any system of nerves or blood vessels; also that all three may on occasion have a wide distribution involving the whole body. Studies were made on the effect of heavy stroking, the histamine reaction and the epinephrine reaction on the skin in normal and affected areas in cases of alopecia areata, vitiligo and scleroderma, respectively. A table is presented showing the detailed record of the observations made. Another table is also given showing the results following the injection of pilocarpine subcutaneously, covering and keeping the patient warm, in order to discover whether any alteration exists in the secretion of sweat on the patches of alopecia areata, vitiligo and scleroderma. In all cases of alopecia areata the response to heavy stroking was substantially the same on the patch of alopecia and on the adjoining normal scalp. The response to histamine on the bald and the normal areas was again substantially

the same. In both instances, however, there was noted a more pronounced tendency in some cases to greater wheal and flare formation on the patches of alopecia areata. This seems to suggest that the tone of the vessels responsible for the color of the skin is less well maintained in the areas of alopecia areata than in the normal areas. The response to epinephrine on the normal and on the bald skin was the same in all cases. The response to pilocarpine by sweating in the cases of alopecia areata was so variable that no certain conclusions could be drawn. The results, however, suggested that there is a tendency for the patches of alopecia areata to sweat less than the normal skin, especially if they are old patches. No difference in reaction to the tests was noted in vitiligo. In scleroderma a reduced flare to histamine on the affected parts was noted. No sweating was noted in the sclerodermatous parts in response to pilocarpine tests. Roxburgh states that his observations reveal no striking or constant difference in the response of the superficial blood vessels to stimuli in skin affected by any of these diseases, as compared with normal skin, although a definite difference apparently exists between scleroderma and the other two conditions, in that patches of scleroderma do not sweat while patches of alopecia areata and vitiligo may do so.

PROGRESSIVE AND RECURRENT DERMATOFIBROSARCOMA (DERMATOFIBROSARCOMA PROTUBERANS). B. USHER, Brit. J. Dermat. **41**:363 (Oct.) 1929.

Two cases of this entity are described as occurring in a man aged 33 and in a woman aged 35. Reports of histopathologic study of tissue from both cases is also presented, with three photomicrographs. Three photographs illustrating the gross picture of the tumor masses are also shown. Reference is made to the other reported cases, with a brief discussion.

PRIMARY SARCOMA OF THE SKIN. H. MACCORMAC, Brit. J. Dermat. **41**:403 (Nov.) 1929.

A case is reported in a woman, aged 48, who presented a tumor in the central portion of the back, about the level of the lower angle of the scapula, which had been present for six months and had gradually increased in size. The whole mass was attached to the deeper structures; there was bilateral axillary adenopathy and practically no subjective sensation. The condition was inoperable. Radium was inserted into the main growth, and the axillary glands were removed. The condition, however, became progressively worse; the patient died ten months after the neoplasm had first been observed. Histologic examination revealed the signs of a sarcoma originating in the derma, and almost complete replacement of adenoid tissue by the growth was noted in the glands invaded by the disease. Two photomicrographs and a colored illustration of the growth accompany the article. The author precedes his case report with a short summary of the literature and gives a classification of primary sarcoma of the skin.

A CASE OF PEMPHIGUS VEGETANS. S. E. DORE and M. MITMAN, Brit. J. Dermat. **41**:408 (Nov.) 1929.

The detailed record of the history and progress of a case in a woman, aged 55, is presented. The authors first saw the patient after she had had the condition about six months and had her under their observation for almost four years, when she died after excision of some of the vegetations in the right axilla. When first seen she presented prominent pinkish cauliflower-like vegetations, accompanied by a fetid, purulent discharge in both axillae, the groins and adjacent abdominal wall, perineum, natal cleft and buttocks. No bullae were noted at this time. *Bacillus pyocyaneus* was the predominant organism found on two occasions. The only gross postmortem observation was fatty degeneration of the heart and liver; examination of the histologic sections revealed changes consistent with those of pemphigus vegetans. The subject of dermatitis vegetans and pemphigus vegetans, respectively, is discussed and brief comments are also made on the etiology of pemphigus vegetans.

In conclusion, the following features are emphasized: (1) the protracted course of the disease; i. e., four and a half years; (2) the maintenance of the general health, which, with few exceptions, did not suggest severe constitutional disease, and (3) the comparative unimportance of the bullae as a clinical feature of the disease and the predominance of the vegetating masses which formed its most striking characteristic. These facts suggested that the case be regarded as pemphigus vegetans in the sense of a distinct clinical entity characterized by the presence of bullae on the skin and the mucous membranes and associated with the development of exuberant papillomatous vegetations rather than that of ordinary pemphigus or dermatitis herpetiformis accompanied by vegetations.

THE TREATMENT OF ERYSIPELAS BY MEANS OF ANTI-SCARLET FEVER SERUM. M. S. THOMSON, Brit. J. Dermat. **41**:417 (Nov.) 1929.

A detailed discussion with case records is presented concerning the use of a serum containing concentrated scarlet fever antitoxin globulins. Reports are given of four cases in which the serum was used successfully and in two cases in infants, aged 3 months and 3 weeks, respectively, unsuccessfully treated with demonstrable septic complications revealed by autopsy. From a study of his cases and the statistics of others the author concludes: 1. The dosage must not be small, but as large as can be given conveniently, particularly in very young infants. 2. The serum must be continued for at least three days and possibly longer, after apparent recovery. 3. In "septic" cases appropriate surgical intervention is essential. 4. All patients who have been treated by this method must be labeled and warned of the absolute necessity of telling their physicians that they have had serum whenever they call him in and whatever the illness may be. 5. It is essential to make up one's mind as to the prognosis early, particularly when the patient is very young or very old. In such cases serum is advisable when great toxicity is obvious and when there is no immediate reaction to the usual forms of treatment. The case must not be allowed to continued for more than two or three days without definite clinical improvement, lest the erysipelas spread to deeper tissues and cause suppuration.

WIEN, Chicago.

DIFFERENT PREPARATIONS OF BISMUTH IN SYPHILIS THERAPY: RATE OF ABSORPTION AS A GUIDE TO THEIR EMPLOYMENT. SVEND LOMHOLT, Brit. M. J. **2**:887, 1929.

An analysis is made with a view to aiding in the selection of the proper preparation. It is pointed out that the internal and percutaneous administration is ineffective because of restricted and irregular absorption of bismuth. The intravenous method is dangerous in large doses, not sufficiently effective in well tolerated doses and impracticable, as it requires frequent injections. The intramuscular treatment is the treatment to be preferred, and its aim is to secure a fairly quick, regular, effective saturation of the body without risk of intoxication. Watery solutions are effective but painful and troublesome, because they require frequent injection. Oily solutions are almost painless, but are not rapidly absorbed. Oily suspensions are generally painless, but their absorption is somewhat slow and often rather irregular. Of this group, in potassium-sodium bismuth tartrate, iodoquinate of bismuth and bismuth salicylate, this is least pronounced. The tartrate has a somewhat varying composition and content of bismuth metal; the iodoquinate has a low bismuth percentage, so that large doses must be given; also, it irritates the tissue. The salicylate has no such drawbacks, and is most suitable for use in an oily suspension. Of the watery suspensions, the oxychloride is the best, because of its purity and stability. Watery suspensions are generally absorbed rather quickly and therefore are painful, but the oxychloride with particles of from 3 to 5 microns is almost painless. The average daily dose of bismuth metal may be fixed at 0.5 mg. per kilogram of body weight. Diffuse storage in the different organs in the body is a matter of slight significance. The unabsorbed deposits are an important factor, and are least dangerous in the intermittent treatment of patients with syphilis.

EPIDERMAL INFECTIONS WITH YEAST-LIKE ORGANISMS WITH SPECIAL REFERENCE TO SEBORRHOEIC ECZEMA. G. B. DOWLING, Brit. M. J. **2**:947 (Nov. 23) 1929.

From dandruff a fungus can be cultivated which when implanted on the skin produces a condition clinically the same as seborrheic dermatitis. It can be recovered from the artificial lesions in scraping or by culture. It appears to be a species of the *Monilia* type of fungus, although it differs from other known pathogenic species of this genus in many respects. Dowling considers it to be the spore of Malassez, because it resembles that spore morphologically. The spore of Malassez is always found in dandruff, and is the only fungus that can be seen inside the scales. It can thus be regarded as the cause of pityriasis capitis for the same reason that *Microsporan furfur* is accepted as the cause of tinea versicolor. And because dandruff is regarded as the starting point of seborrheic dermatitis, the spore of Malassez is concerned in the production of seborrheic dermatitis.

There is a short discussion of the botanical position of the various organisms causing epidermomycoses and a critical consideration of the work done by other men on the same problem — notably the work of Benedek, who considers the so-called seborrheic eczemas to be due to the fungus species *Ascomycetes*.

RATTNER, Chicago.

MICROSPOROSIS AND TRICHOPHYTOSIS OF THE SCALP IN ADULTS. G. MASSIA and J. ROUSSET, Ann. de dermat. et syph. **10**:828 (Aug.) 1929.

The authors report a case of tinea capitis in a woman, aged 30 years, who was probably infected by her child. *Microsporon lanosum* was cultivated from both patients. Tinea capitis in adults is a well known rarity; the authors were able to collect from the literature only nineteen cases due to *Trichophyton*, and three produced by *Microsporon*. (This compilation is incomplete, at least as far as the American literature is concerned.) The commonest *Trichophyton* encountered in adult cases was *Trichophyton violaceum*. *Microsporon audouini* was probably present in the cases of microsporosis found in the literature, whereas the authors' case was due to *Microsporon lanosum*. In some cases the disease of the scalp began in childhood, while in others the source of infection was a child with the disease. Several cases have appeared during lactation, thereby suggesting a hypofunction of the gonads as a predisposing factor. The endocrinologic factor in adult cases is obscure but probably important. The treatment for adults is the same as that for children.

DERMATONEUROMA. D. MOSTO, Ann. de dermat. et syph. **10**:845 (Aug.) 1929.

Mosto had an opportunity to examine pathologic specimens from a case that clinically corresponded to those described by Darier and Ferrand as progressive and recurrent dermatofibroma or fibrosarcoma of the skin. He does not agree with those authors in their classification of these cases. He believes that they are cutaneous neuroma. The histologic structure corresponded to fibroma with a dense cellular structure, but between the connective tissue fibers were seen many elongated cells with a fine granular protoplasm, colored red with van Gieson stain. Pathologically, there is no suggestion of malignancy. From the results with special staining, the author concludes that the tumors are composed of nerve tissue chiefly, and that the fibrous element is secondary. Therefore, they are cutaneous neuromas, or better, Schwannomas or peripheral gliomas.

ARE THE FIBROSARCOMAS OF THE SKIN REALLY NEUROMAS? APROPOS OF THE ARTICLE BY D. MOSTO. J. DARIER, Ann. de dermat. et syph. **10**:852 (Aug.) 1929.

Darier was asked by the editors of the *Annales* to comment on the foregoing article by Mosto. He agrees that Mosto's case was similar to those described by Ferrand and himself. The disorder is characterized by firm, projecting, fibrous masses usually located on the abdomen or in the groin.

Darier does not accept Mosto's interpretation of the tumors as neuromas. Mosto's tinctorial methods are subject to criticism and his conception of the secondary rôle of the connective tissue element in the sections is rejected by Darier. Until better evidence is produced, Darier believes that his original designation of fibrosarcoma must stand.

OBSTINATE GENERALIZED ECZEMA CURED BY NON-SPECIFIC DESENSITIZATION. N. N. DRACOULIDES, Ann. de dermat. et syph. **10**:864 (Aug.) 1929.

The author reports a severe case of generalized eczema in which the definite cause was undetermined, but was probably of systemic origin. There was a slow but progressive recovery under autohemotherapy, intravenous injections of calcium chloride and opotherapy.

PAINFUL NODULE OF THE EAR. G. BELGODERE, Ann. de dermat. et syph. **10**:873 (Aug.) 1929.

Belgodere briefly reports a case of painful nodule of the ear in a man aged 57.

PHOSPHORUS DERMATITIS. J. NICOLAS, J. GATE and J. ROUSSET, Ann. de dermat. et syph. **10**:921 (Sept.) 1929.

The authors give an extensive clinical and experimental report on occupational dermatitis occurring among employees of a match factory. The disease is due to phosphorus sesquisulphide. The lesions develop rapidly, first on the exposed parts, but soon become generalized. The eruption is erythematous primarily but rapidly becomes vesicular or pustular. Occasionally, small necrotic areas appear. The outbreak is accompanied by severe subjective sensations. The attack rapidly subsides. A severe conjúnctivitis is often present.

The authors produced the eruption in volunteers with a paste containing phosphorus sesquisulphide. Similar results were obtained in experimental animals.

Pathologically, the lesions presented a banal dermatitis of varying intensity. The powdered chemical alone seems capable of producing cutaneous lesions and requires intimate contact with the skin before deleterious effects occur. Oxidation likewise plays a rôle. Greasy skins are more susceptible than dry ones.

As the chemical in powdered form is most dangerous, industrial plants using phosphorus should install machinery to prevent its diffusion in the air. Workers should also wear special garments which prevent the powdered phosphorus sesquisulphide from reaching the skin. For the eruption, a watery solution of potassium permangenate and sodium bicarbonate is indicated.

A CASE OF LUPUS VULGARIS DUE TO AVIAN TUBERCLE BACILLI. S. NICOLAU and M. BLUMENTHAL, Ann. de dermat. et syph. **10**:953 (Sept.) 1929.

The patient, a youth, aged 19, had a typical case of lupus vulgaris with patches of the disease on the face, neck and right wrist. Bacteriologic study of the organism recovered from the lesions, which is reported in detail, proved its avian origin. Tuberculosis of the skin due to the avian strain are rare; the authors found but three reported cases. In these cases the lesions were ulcerative, while in the authors' cases they were of the tumidus and nonulcerative variety.

LEISHMANIASIS OF THE GENITALS. F. SILVA, Ann. de dermat. et syph. **10**:965 (Sept.) 1929.

Three cases of this disease in which the genitals were affected are described by Silva. The disease is most common on the exposed parts, but no cutaneous area is exempt. In the reported cases, the organism was identified by laboratory examinations. Injections of tartar emetic gave satisfactory therapeutic results.

MICHAEL, Houston, Texas.

TUBERCULOUS BUCCAL ULCERATIONS. CHOMPRET and DECHAUME, Bull. Soc. franç. de dermat. et syph. **36**:623 (July) 1929.

A case of tuberculosis orificialis was presented with the unusual feature of lesions over the lower mandible.

SQUAMOUS VARIETY OF PALMAR AND PLANTAR EPIDERMOPHYTOSIS DUE TO EPIDERMOPHYTON OF PRIESTLEY. P. PHOTINOS, Bull. Soc. franç. de dermat. et syph. **36**:625 (July) 1929.

In this case, the lack of vesiculation, limitation to the palms and soles, and an organism cultured from the scales were features of interest.

CHANCRE OF THE CONJUNCTIVA IN A PHYSICIAN. LOUSTE and THIBAUT, Bull. Soc. franç. de dermat. et syph. **36**:629 (July) 1929.

The reporters presented the case because of the rarity of the location of the initial lesion and the failure to suspect its real nature until the development of secondary lesions.

DUHRING'S DISEASE: CONJUNCTIVAL BULLAE. LOUSTE and PINOCHE, Bull. Soc. franç. de dermat. et syph. **36**:633 (July) 1929.

The patient, presented in 1924, was again presented to show the cicatrices and evolution of the conjunctival lesions. The conjunctiva had become completely epidermized.

PRIMARY MELANODERMA. MILIAN and NATIVELLE, Bull. Soc. franç. de dermat. et syph. **36**:635 (July) 1929.

An Algerian, living in France for three years, presented a marked melanoderma of the face. Addison's disease, melanosis of Riehl, etc., were ruled out as causes.

GENERALIZED ZOSTER. LORTAT-JACOB and POUMEAU-DELILLE, Bull. Soc. franç. de dermat. et syph. **36**:642 (July) 1929.

A case of right brachial zoster with associated disseminated lesions was presented.

A GENERALIZED CHRONIC PAPULAR ERUPTION APPEARING IN CONJUNCTION WITH ACUTE ARTICULAR RHEUMATISM. MILIAN and G. GARNIER, Bull. Soc. franç. de dermat. et syph. **36**:643 (July) 1929.

A young girl with acute arthritis developed a profuse, disseminated papular eruption offering considerable diagnostic difficulty. Biopsy showed tuberculoid structure, and the diagnosis of papular tuberculid was made.

ATROPHIC SYPHILIDS. M. PINARD and RABUT, Bull. Soc. franç. de dermat. et syph. **36**:647 (July) 1929.

A macular syphilid, on involution, left atrophic patches.

LEPROSY TREATED WITH MALARIA THERAPY. M. PINARD, RABUT, GIRAND and ABRICOSOFF, Bull. Soc. franç. de dermat. et syph. **36**:648 (July) 1929.

A patient with leprosy evoluting fairly acutely, despite treatment with chaulmoogra oil, was treated by impaludation. After seven febrile attacks, the malaria infection spontaneously disappeared. There was a definite, but transitory, improvement in the leprous lesions.

EARLY MAMMARY PAGET'S DISEASE INVOLVING THE LACTIFEROUS DUCTS. COEXISTENCE OF DEEP CANCER OF THE BREAST. G. BARBIER, Bull. Soc. franç. de dermat. et syph. **36**:649 (July) 1929.

In Barbier's patient there was an insignificant surface lesion of several months' duration, but a palpable nodule in the breast. Complete amputation of the breast

showed that there was present Paget's disease of the nipple with two lactiferous ducts filled with malignant cells, and a cancerous mass in the depths of the breast. In this case, it seemed likely that the malignant change had developed primarily in the deeper mammary tissue and subsequently reached the surface.

BISMUTH RETENTION ABSCESS FOLLOWING A TRAUMATISM. J. ROBERTI, Bull. Soc. franç. de dermat. et syph. **36**:652 (July) 1929.

Roberti's patient had received a course of bismuth in 1925. In 1928 he suffered severe injuries in an automobile accident and in the following two weeks developed a gluteal abscess which continued to discharge until it was incised and curetted. Solid particles obtained from the discharge and curettings were chemically identified as bismuth in organic form.

EXFOLIATION THERAPY IN ACNE BY MEANS OF A MIXTURE OF CARBON DIOXIDE SNOW, ACETONE AND SULPHUR. GIRAUDEAU, Bull. Soc. franç. de dermat. et syph. **36**:654 (July) 1929.

The ingredients are mixed to form a paste which is applied by rapid friction without pressure. The sulphur which is deposited is left on the skin for a half hour. The author has used the method with satisfaction for several years.

MICHAEL, Houston, Texas.

MALIGNANT EPITHELIOMA OF THE SWEAT GLANDS. A. CROSTI, Gior. ital. di dermat. e sifil. **70**:768 (Aug.) 1929.

Epitheliomas of the skin arising in the sweat glands are rare and can be diagnosed only after a thorough study of their histologic structure. Of thirty cases reported, at least ten are of doubtful diagnosis.

In the majority of cases the tumors develop spontaneously, or after a slight trauma, as a small nodule which grows slowly. Occasionally the tumor may develop on a preexisting adenoma, as in one of the two cases reported by the author. Ulceration rarely occurs. The seat of the tumor or tumors is usually the face, but cases have been reported in which it was the neck, thorax, arms, legs and vulva.

Although the lesions develop slowly, they may cause lymphatic metastasis, and death may be the end in some cases.

Histologicaly, the structure of these epitheliomas may be said to be polymorphous, with tubular or cystic cells predominating and basocellular and even spinocellular groups of cells present. Hyaline and mucous degeneration of the cells is a frequent occurrence. Points of interest in the diagnosis are the deep situation of the tumoral mass, the lack of relation between the tumor and the cells of the epidermis, the hair follicle and the sebaceous glands, and the general microscopic appearance of the tubular or tubulocystic epithelium, recalling sometimes the lesions of hydro-adenoma.

INFANTILE ACRODYNIA. MARIO ARTOM, Gior. ital. di dermat. e sifil. **70**:810 (Aug.) 1929.

The author reviews the history of this disease, comparing the epidemic condition in adults and the newly described infantile form of the disease. He reports three cases observed by him in Novara, Italy, and describes in detail the psychic, neuromuscular, cutaneous and mucous symptoms. He deals at length with the question of differential diagnosis of arsenical poisoning, pellagra and ergotism.

From his studies and observations, the author concludes that acrodynia is due to a diffuse involvement of the neuro-axis and of the vegetative system produced by a virus still unknown but probably similar to the germ of epidemic encephalitis and of poliomyelitis — i. e., a neurotropic virus.

HYPERGLYCEMIA IN RELATION TO DISEASES OF THE SKIN AND TREATMENT WITH INSULIN. F. NARDUCCI, Gior. ital. di dermat. e sifil. **70**:857 (Aug.) 1929.

The author reports his studies on the relation between hyperglycemia and several diseases of the skin in sixty-six cases. He employed the Folin-Wu method, performing his tests in the early morning before breakfast and also from two to three hours after the patient had drunk a cup of coffee and milk. He found results above normal in eighteen of thirty-nine cases of eczema, in eight of ten cases of psoriasis, in three of seven cases of furunculosis and in one of ten other cases of dermatosis. Treatment with insulin was encouraging, particularly in the cases of eczema; in the latter group he treated fifteen patients, with recovery in ten and improvement in two.

BIOLOGIC ACTION OF THALLIUM ACETATE. G. TRUFFI, Gior. ital. di dermat. e sifil. **70**:872 (Aug.) 1929.

This article is in response to that of Buschke and Peiser concerning the mode of action of thallium salts on the hair. Truffi insists that the most logical explanation for the alopecia produced by thallium is that the drug acts directly on the hair follicle; he believes that a primitive action on the sympathetic system is hypothetic, and without foundation.

CUTANEOUS AND NERVOUS SYPHILITIC LESIONS COEXISTING IN THE SAME PATIENT. B. CARTIA, Gior. ital. di dermat. e sifil. **70**:887 (Aug.) 1929.

This is a report of a clinical case in which tabes dorsalis was coexistent with gummatous ulcers of the legs. The author favors the theory of the unity of syphilitic spirochetes.

PURPURA ANNULARIS TELANGIECTODES (MAJOCCHI). L. MARCHISIO, Gior. ital. di dermat. e sifil. **70**:892 (Aug.) 1929.

The author reports a case of typical Majocchi's disease in a man aged 26, in whom no signs of tuberculosis could be found. He refutes the assertion of many investigators, among them Balzer, who claim that Majocchi's disease belongs among the tuberculids. The disease seems to be of toxic origin, and in the case reported, poisoning with mercuric chloride seems to have been the etiologic factor.

EPIDERMOLYSIS BULLOSA DYSTROFICA WITH HEMATOPORPHYRINURIA. A. MARCOZZI, Arch. ital. di dermat. e sifil. **4**:355 (July) 1929.

The author reports the case of a boy, aged 6 years, in whom two prominent features were hematoporphyrinuria and erythrodontia. The patient presented hyperhidrosis palmaris and hypertrichosis. A congenital condition was suggested, perhaps affecting the endocrine function, but no definite etiologic factors were elicited from the study of this case.

MELANODERMA DUE TO ACRIFLAVINE HYDROCHLORIDE. E. ALVAREZ SAINZ DE AJA, Progresos de la clin. **37**:485 (Aug.) 1929.

The patient was a young woman, aged 19, who had been under treatment with intravenous injections of acriflavine hydrochloride for a blenorrhagic infection. About a month and a half after the beginning of this treatment, the patient developed an intense melanoderma of the face and hands. The author believes that the dye sensitizes the skin to the solar rays.

PARDO-CASTELLO, Havana, Cuba.

DERMATOLOGIC ABSTRACTS

The Journal of the American Medical Association

Treatment of Neurosyphilis. H. C. Solomon, Ann. Int. Med. **3**:447 (Nov.) 1929.

Solomon states that a conservative summary of the literature of the world concerning the results obtained with malarial treatment indicates that a thoroughly good clinical result is obtainable in about 30 per cent of the cases of paresis, while approximately another 30 per cent show a reasonable amount of improvement. Complete tabulation of the results obtained in the treatment of paretic cases by tryparsamide is not available, but what information is at hand would indicate that results are substantially the same as obtained by the use of malaria. The important factor to be stressed is that with both these methods it is possible to obtain complete serologic recovery in a considerable number of cases. Long-continued treatment is many times required to produce a serologic recovery. It is Solomon's usual custom when using tryparsamide to continue it indefinitely and usually without interruption until the desired result is at hand. Having sufficient optimism to believe that a serologic recovery is nearly always available, he perseveres, however long it may take, week after week, month after month, and year after year. The highest number of tryparsamide injections which he has given to any one patient is 183 in a period of little less than five years. There is rarely any evidence of cumulative effects or lack of ability of patients to handle the drug.

Intracisternal Treatment of Neurosyphilis. C. R. Rayburn and D. W. Griffin, J. Oklahoma M. A. **22**:389 (Nov.) 1929.

Rayburn and Griffin report their experience with this treatment in twenty-two cases, in which 119 punctures with intracisternal medication have offered no complaints, and no complications of any importance have been noticed. Headaches following the punctures and treatments have been negligible, and "nil" when comparing them to the postpinal headaches which are so frequent after simple drainages from the lumbar region.

Acute Sensitization in Infant to Cow's Milk Protein. H. T. Ashby, Arch. Dis. Childhood **4**:264 (Oct.) 1929.

In the case described by Ashby, eczema developed at the age of 3½ months, possibly because of the foreign protein of the milk taken by the mother passing through into the human milk. The baby gave a mild positive skin reaction to the mother's milk. The process of desensitization consisted in giving minute doses of cow's milk at the start and gradually increasing the dose day by day. The increase of dose is governed by the ability of the infant to take the quantity of milk without developing any reaction. If a reaction such as urticaria or irritability is noticed, the dose must be kept the same for a time or even reduced for a day or two. In an extreme case it is wise to go slowly and not to hurry, as a setback is serious and prolongs the desensitizing time. Later on, the rate of increase of the milk can be made more quickly. For the immediate treatment and relief of the acute symptoms a hypodermic injection of epinephrine (1:1,000) should be given.

Early Diagnosis of Latent Heredosyphilis. A. G. Alarcon, Arch. de méd. d. enf. **32**:589 (Oct.) 1929.

Alarcon reports a new clinical guide in the diagnosis of heredosyphilis, on the basis of a typical intestinal disorder occurring in infants under 3 months of age. This was named "transitional dyspepsia of infants" by the author and

is characterized by the symptoms occurring after the first days of breast feeding. For some time after feeding, regurgitations and hiccups occur, at times even waking the infant. Its intestinal discomfort is voiced by crying. Vomiting is rare in breast-fed infants though frequent in cases of artificial feeding. Acid diarrhea, with gluteal erythema, follows the period of constipation. Alarcon distinguishes between a preliminary stage lasting three weeks, a second stage lasting six weeks and a final stage of reduction also lasting three weeks. Although other parasitic infections, such as malaria and amebiasis, may be conducive to similar symptoms, Alarcon considers the influence of syphilitic septicemia on the nervous system of the infant to be the most frequent cause. Of especial value in the differential diagnosis are the early onset, the exaggeration of the symptoms and as a guide toward the diagnosis of syphilis a duration of the condition beyond ninety days.

ELASTICITY OF SKIN IN CANCER. H. GUTHMANN and A. ERB, Arch. f. Gynäk. **138**:269 (Sept. 20) 1929.

In determinations of the elasticity of the skin in twenty healthy persons and in twenty persons with cancer, Guthmann and Erb noted a marked decrease in the elasticity of the skin in the persons with cancer. The decrease was definite even in beginning carcinomatous processes.

RELATION BETWEEN LEUKOPLAKIA AND KRAUROSIS OF VULVA. E. TERRUHN, Arch. f. Gynäk. **138**:318 (Sept. 20) 1929.

According to Terruhn, leukoplakia vulvae is not a disease entity but is only a symptom of the first stage of kraurosis vulvae.

HERPES ZOSTER FOLLOWING RECOVERY FROM CHICKENPOX. K. DIETL, Wien. klin. Wchnschr. **42**:1078 (Aug. 15) 1929.

Dietl states that, according to most authorities, varicella and herpes zoster are essentially alike. He reports two cases of herpes zoster. In these instances the disease developed in children who, in previous years, had passed through an attack of varicella. These cases demonstrate that the immunity following a varicella infection is not absolute. They also show that an organism which is partially immune against varicella may still contract herpes zoster. It is stressed that in the one instance the earlier varicella infection had been only slight. The disease did not make the child allergic rather than immune, and in this allergic organism the new varicella infection resulted in an eruption that had the character of a herpes zoster.

TREATMENT OF PSORIASIS WITH EXTRACT FROM PSORIATIC CUTANEOUS SCALES. V. MIHAJLOVIĆ, Wien. klin. Wchnschr. **42**:1192 (Sept. 12) 1929.

In the treatment of ten patients with psoriasis, Mihajlović employed an extract that was prepared by digesting psoriatic cutaneous scales with pepsin and trypsin. His observations are summed up as follows: The subcutaneous injection of this preparation causes neither local nor general reactions. In the beginning of this treatment the skin itches and the scales peal more quickly and more easily. In the course of this treatment the punctate hemorrhages that otherwise develop after the removal of the scales do not appear. The painfulness of the joints disappears. In nearly all patients who underwent this injection treatment, leukoderma developed. The leukodermic areas occur in the same place and have the same shape as the psoriatic lesions. After the treatment is begun, the lesions on the scalp, on the chest and on the abdomen are usually the first ones to disappear, whereas those on the knees and the elbows are generally more refractory. The injections are given subcutaneously, in quantities of from 1 to 10 cc., and after intervals of from one to five days. The extract may be prepared either from the patient's own scales or from those of other patients. In most instances better results were

obtained with analogous extracts. This method of therapy does not always prevent the occurrence of relapses. However, the author thinks that the favorable results which were gained with this treatment prove that it deserves to be further investigated.

SKIN DISEASES IN CHILDREN: THEIR RELATION TO INTERNAL DISTURBANCES. C. LEINER, Wien. med. Wchnschr. **79**:1139 (Aug. 31) 1929.

Leiner describes various forms of skin diseases that occur in infants and children. He shows that dermatitis generally appears as a result of an internal disturbance. He traces toxic erythema neonatorum to dyspepsia, to inflammatory processes in the oral cavity or to toxic influence during the prenatal period. Other skin diseases in infants and children are the result of septic processes. The author mentions particularly ecthyma gangrenosum. Nutritional disturbances often lead to furunculosis or to ecthyma cachecticorum. A form of scurvy often becomes manifest in children whose food is deficient in vitamin C. The skin of such patients is pale and sallow and shows hemorrhagic areas. The author further mentions ammonia dermatitis, which is localized mainly in the gluteal region. It is caused by *Bacillus ammoniagenes*. Another dermatitis of the gluteal region is often observed in children with thrush. This form is caused by *Monilia albicans*. Strophulus, probably the most common skin disease in infants and children, usually affects overnourished children with gastro-intestinal disturbances and constipation. A macular exanthem is frequently noted in children with pyelocystitis. Pseudojaundice becomes manifest in infants who have been fed with carrots. In cases of inflammation of the cardiac valves, erythema gyratum often develops and erythema annulare is noted in patients with acute endocarditis. Erythema multiforme becomes manifest after an angina, in the course of articular rheumatism. Tuberculosis in children is often accompanied by erythema nodosum. Other skin diseases that are noted in tuberculous children are the various forms of lupus and of scrofuloderm, and also miliary tuberculosis. Diseases of the central nervous system are also frequently accompanied by skin diseases. In epidemic encephalitis a macular exanthem is often noted, and adenoma sebaceum occurs with tuberous sclerosis. Finally the author again stresses the fact that the skin is the mirror of the internal processes. In short, a dermatitis is generally the result of an internal disturbance.

PSEUDOPOSITIVE WASSERMANN REACTIONS IN INFANTS LESS THAN TWO WEEKS OLD. L. LEMEŽ, Ztschr. f. Kinderh. **48**:97 (July 20) 1929.

In 271 new-born infants, Lemež examined blood from the umbilical cord and from the heel (obtained following cleaning of the heel with ether by making an incision 3 mm. long and from 0.5 to 0.75 mm. deep in the lateral distal third) as follows: Wassermann reaction 708 times, Sachs-Georgi test 311 times, Meinicke test 388 times and Mueller's conglobation reaction 344 times. In most of the cases the blood was examined serologically on the third day of extra-uterine life and again a few days later. The Wassermann reaction was positive in 18 per cent of the cases at the first examination; in most of the cases the reaction became negative after from three to five days. The author believes that the pseudopositive Wassermann reaction is caused chiefly by the increased lability of the serum, which manifests itself in the rapid decrease in the serum-globulin during the first ten days of life. In the first two weeks of life both nonsyphilitic and syphilitic infants may give nonspecific Wassermann reactions. Healthy new-born infants of syphilitic mothers who give a positive Wassermann reaction in only the first two weeks of life are to be considered as having been born free from syphilis, as long as they remain clinically healthy and the Wassermann reaction is negative. The irregularities in the Wassermann reaction in congenital syphilis are caused by the fact that at first nonspecific reactions and later specific reactions occur. The author believes that because of the large number of nonspecific reactions it is not advisable to perform the Wassermann test with the blood of infants during the first eighty days of life.

Society Transactions

SAN FRANCISCO DERMATOLOGICAL SOCIETY

H. J. TEMPLETON, M.D., *Secretary*

April, 1929

ERNEST CHIPMAN, M.D., *Chairman*

LUPUS VULGARIS. Presented by DR. MAYNARD.

A woman, aged 44, presented a semicircular lesion of eighteen years' duration over the right external malleolus. There was some pruritus. During the daytime, the characteristic apple-jelly nodules and scarring could be seen. The patient would not permit a biopsy because of the extremely slow healing of a previous wound in this area. It was intended to try gold sodium thiosulphate as a patient at Stanford University had shown considerable improvement of lupus vulgaris and tuberculous dactylitis under therapy with a gold compound.

DISCUSSION

DR. MORROW: This is a case of chronic eczema of the leg. There is no reason to diagnose it as lupus vulgaris. Has any roentgen therapy been applied?

DR. CULVER: This condition is chronic eczema, and the scarring is probably due to secondary infection.

DR. ALDERSON: If therapy with a gold compound is used as a test measure, one must remember that many other chronic infiltrations will clear up under this sort of therapy.

DR. CHIPMAN: This patient presents certain points of destruction and scarring which would not be seen in eczema.

EPITHELIOMA DEVELOPING ON LUPUS VULGARIS. Presented by DR. LIGHT for DR. ALDERSON.

A woman, aged 24, presented a lesion of lupus vulgaris with a small epithelioma arising from it, located beneath the left lower eyelid, of eight years' duration. The lupus was of much longer standing. Because of the slight amount of ectropion already present, a biopsy was feared. The clinical diagnosis was apparent.

DISCUSSION

DR. MORROW: This is a classic basal cell epithelioma of the cicatrizing type. I should suggest roentgen therapy.

DR. CHIPMAN: I can recall a case which was clinically lupus vulgaris but in which biopsy showed a basal cell epithelioma.

DR. MILLER: If this condition was originally lupus vulgaris, it would be rare for it to degenerate into a basal rather than a squamous cell epithelioma.

DR. CLARK: I would suggest treating it with pure phenol.

DR. TEMPLETON: I have treated several similarly situated epitheliomas with electrodesiccation and the roentgen rays and so far have not had ectropion develop.

DR. TAUSSIG: It would be well to try radium first; if it fails, then electrodesiccation would be in order. Radium is controlled more easily than the roentgen rays.

DR. MILLER: I would differ from Dr. Taussig in believing that radium is more easily controlled than the roentgen rays.

DR. STRATTON: Dr. Fordyce used electrolysis on this type of epithelioma when it occurred on the eyelids, with good results.

MULTIPLE IDIOPATHIC KELOIDS OF THE CHEST AND BACK. Presented by DR. MILLER.

One keloidal lesion of the back was excised in 1912. This was followed within two weeks by the appearance of many new lesions. At present there are symmetrical, dumbbell-shaped lesions over the back and chest. The possibility of their being the Darier-Roussy type of sarcoid was considered but a biopsy showed them to be fibromas.

DISCUSSION

DR. CULVER: The symmetry would make one think of the possibility of their being secondary to excoriations from pediculosis corporis.

LYMPHANGIOMA CIRCUMSCRIPTUM OF TONGUE. Presented by DR. H. J. TEMPLETON.

Miss———, aged 21, at the age of 7, while living in Hawaii, first noted "blisters" on the tongue. More had gradually appeared until at the time of presentation practically the whole tongue was covered with groups of transparent grape-like bodies about from 2 to 4 mm. in diameter. Some were pedunculated. When pricked with a needle, they collapsed and a clear sticky fluid exuded. They were not painful or tender. There was no enlargement of the glands of the neck. Therapeutic suggestions would be appreciated.

DISCUSSION

DR. MORROW: I should suggest gradual destruction with a fine pointed cautery.

DR. TAUSSIG: Radium therapy is not indicated.

DR. MILLER: Although this growth is evidently of lymphatic origin, I am somewhat in doubt as to the correctness of the classification.

SQUAMOUS CELL EPITHELIOMA. Presented by DR. REYES for DR. WAY.

T. G., aged 46, a welder, entered Stanford Clinic on Feb. 25, 1929, complaining of a tumor on the nose. About one year before presentation he received a blow on the nose, and the swelling from this injury did not subside but continued to increase slowly and to become harder. The lesion was located chiefly on the left side of the nose, partially obstructing the vision of the left eye. It was about 2 by 3 cm., very firm and without ulceration or bony attachment. The Wassermann reaction was strongly positive. Several surgeons saw the case in consultation but failed to recognize it as malignant. They advised that intensive syphilitic treatment be tried before biopsy was attempted. The patient was given iodides in increasing doses, and he received two injections of bismuth. The day of presentation was the first time that the patient had been seen for a month. In the meantime, the lesion had increased from 2 by 3 cm. to 4 by 6 cm.

DISCUSSION

DR. CHIPMAN: I remember that Professor Gauchet feared the use of iodides in malignant conditions.

DR. MORROW: This is a typical squamous cell epithelioma.

A Case for Diagnosis. Presented by Dr. Maynard.

A man, a dairy truck driver, had an ichthyotic skin and also lesions on the dorsum of the hands suggestive of allergic dermatitis. These occurred in cycles. He had had nearly all possible varieties of treatment in the last fifteen years. Five different cultures had yielded a black mold. He improved under the use of tar.

DISCUSSION

Dr. Miller: This is probably an epidermomycosis on an ichthyotic background. The fact that it becomes worse when treated with the roentgen rays argues in favor of ichthyosis.

Dr. Templeton: Let Dr. Taussig try his Grenz ray.

Dr. Taussig: The Grenz ray would have the same effect as the roentgen ray.

Parapsoriasis (Brocq Type). Presented by Dr. Chipman.

A man, aged 55, presented erythematosquamous patches on his arms and trunk of two years' duration. He had received treatment for chromophytosis from another physician without benefit. The lesions practically disappeared when he was treated with ultraviolet light but reappeared when the light was discontinued. They were somewhat pruritic.

DISCUSSION

Dr. Templeton: The pruritus would make one want to consider the possibility of this being the premycotic stage of mycosis fungoides. I recall a case presented by Dr. Klauder in which the original diagnosis of parapsoriasis en placques had to be changed later to mycosis fungoides.

Dr. Chipman: Pruritus was absent until treatment was instituted.

Dr. Morrow: The configuration suggests mycosis fungoides.

Two Cases of Erythema Induratum. Presented by Dr. Torrey.

A girl, aged 20, presented typical Bazin's disease. She had chorea at 8 and again at 11 years of age. The trouble present at the time of presentation began when she was 11. She had parenchymatous pulmonary tuberculosis and mitral heart disease. She had received gold sodium thiosulphate, tuberculin and sodium cacodylate. Another patient, a girl, had classic Bazin's disease also, but was robust and healthy.

DISCUSSION

Dr. Miller: The last patient developed focal reactions when treated with tuberculin, but later improved.

Dr. Alderson: I recall one patient with typical Bazin's disease who showed marked improvement under the use of tin oxide locally and by injection (given by a physician in Honolulu). I am not prepared, however, to recommend this agent. We have had success with injections of a gold compound and quartz lamp therapy.

Papulonecrotic Tuberculid. Presented by Dr. Chipman.

A man, aged 33, developed lesions on the feet and legs in 1918 while in the French army. His condition was diagnosed as "trench foot." New lesions had appeared intermittently since then. A tuberculin reaction was strongly positive. The individual lesions were papules which developed a necrotic center.

DISCUSSION

Dr. Alderson: I agree with the clinical diagnosis, but I should like to see sections of a lesion.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, May 15, 1929

H. R. FOERSTER, M.D., *President, Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. ORMSBY.

A boy, aged 19, had a disorder of one year's duration. The eruption began on the neck, and spread from there over the trunk and upper extremities. No subjective symptoms had been present. The eruption has not been affected by treatment or by other agencies.

Examination showed an eruption on the back, on the sides of the neck, on the arms, on both sides of the chest and on the abdomen, consisting of follicular, reddish-brown papules the size of a pinhead. Some of the lesions showed a central hair, and all were covered by scales or by slightly greasy crusts. On the neck, confluence of the papules had occurred to produce small patches. Much greasy scaling was present in the scalp. There were no abnormalities aside from those of the skin.

DISCUSSION

DR. WILE: I think it is difficult in this case to make a correct diagnosis. A few things occurred to me as possibilities that should be considered. One, that it was an unusual disseminated follicular tuberculid; another, that it was a pityriasis rubra pilaris which had begun in an unusual way.

DR. FOERSTER: What impressed me was the peculiar character of the lesions. I considered the possibility of a lichen planus pilaris, of a tuberculid and of pityriasis rubra pilaris. The absence of spines, I understood Dr. Ormsby to say, is recent, the spines having vanished under treatment. I cannot make a definite diagnosis.

DR. ORMSBY: I think the diagnosis cannot be settled at this time. Pityriasis rubra pilaris, to my mind, comes first. Originally Darier's disease was considered, but now I think that it can be ruled out. There were definite spines on the neck, but they have disappeared. We will try to get a biopsy and report the observations later.

A CASE FOR DIAGNOSIS. Presented by DR. ORMSBY.

A man, aged 33, had a disorder of ten years' duration. The lesions began as small spots, but gradually increased in size. No new areas had developed during the last four years. As the margin advanced, the center cleared. From time to time the lesions were more or less conspicuous.

At the present time the disorder was limited to the forehead, and occurred as three or four circular areas with a clearing center. The margins were slightly elevated and bluish-red. The diameters of the larger lesions were about 2 inches. The center of the area was pink, and suggested atrophy. A permanent brown discoloration was shown in the margins under diascopic pressure. The differential blood count showed no abnormality. The Wassermann reactions had been contradictory, positive in some laboratories and negative in others.

DISCUSSION

DR. SENEAR: I have no diagnosis to offer, but I thought of leprosy, syphilis and some form of tuberculosis of the skin. I felt that there was some definite brownish infiltrate left under diascopic pressure, but it did not look like tuberculosis to me.

DR. STILLMANS: I thought of the same things Dr. Senear mentioned, and I rather favor tuberculosis, because of the brownish tint under the diascope.

DR. WILE: I think one should consider, in addition to the things mentioned, an unusual form of erythematous lupus. There was no infiltration and no scaling, but I think occasionally forms of lupus are seen in which these may be absent altogether with the absence of atrophy. I recall one definite case of erythematous lupus in which one would expect atrophy, but none was found. The lesions have spread as erythematous lupus sometimes does.

DR. MITCHELL: I was particularly struck by the resemblance of these lesions to those in a Chinese patient demonstrated several years ago. I never was able to prove that it was leprosy, although the histology strongly suggested that disease. We never found the organisms in the nasal smear. I also thought of lupus erythematosus, but it seemed to me the appearance of the lesions was against that diagnosis.

DR. FOERSTER: Aside from the conditions that have been mentioned I thought of granuloma annulare. It presents certain features of that disorder. There is an edema, it seems to me, in the absence of a section, which appears to speak more for granuloma annulare.

DR. OLIVER: When I first saw this patient I thought the lesion bore a great deal of resemblance to maculo-anesthetic leprosy, but there is no anesthesia in the patches. Under the diascope its apple-jelly brown appearance made me think of an unusual type of lupus.

DR. LIEBERTHAL: I think the only possibility that has not been suggested is a septic condition, and this should be considered.

DR. EBERT: I thought it might be an annular form of Boeck's sarcoid, which would put it in the tuberculosis category, because of the slow rate of spread, the nodular border and the color.

DR. MONTGOMERY: I saw a patient recently with a solitary lesion on the back that resembled a granuloma annulare or superficial epitheliomatosis. The histopathologic picture, however, was definitely that of a sarcoid, the section being composed of numerous epithelioid tubercles and there being no microscopic evidence of epithelioma nor of granuloma annulare. Dr. Goeckerman and I, therefore, made a final diagnosis of annular sarcoid.

DR. ORMSBY: I believe it is the type of lupus vulgaris described originally by Leloir, in 1891, under the title lupus erythematodes. His idea was that there was a borderline type between lupus erythematosus and lupus vulgaris. In a patient seen several years ago similar lesions were present over the nose and cheeks, and a biopsy revealed the histologic architecture of lupus vulgaris. When this patient was first seen lepra, syphilis and some form of tuberculosis were discussed. By therapy, serologic tests and further study, the first two were ruled out. We have not yet been able to obtain a biopsy but will probably do so.

A CASE FOR DIAGNOSIS. Presented by DR. OLIVER.

S. G., a white man, aged 26, complained of an eruption in the left groin of two years' duration. Its onset was preceded by an acute scaling dermatitis on both palms which responded to alpine sunlight therapy.

The cutaneous eruption was a brownish-yellow area, the size of a palm, and was covered with a fine scale. Itching at times was intense. All sorts of treatment, including roentgenotherapy, Whitfield ointment and sulphur ointment had failed to relieve him.

DISCUSSION

DR. MITCHELL: I was much interested in this case, and I believe I have never seen anything just like it. The pigment was not dark enough for erythrasma, and it is difficult to demonstrate *Microsporon minutissimum*. Whether *Sarcinae* are etiologic factors I do not know. I have found them repeatedly in cultures, but have disregarded them because I was looking for fungi rather than for bacteria.

DR. WHITE: So far as the bacterial observations are concerned, I think the only absolute proof of pathogenicity would be to inoculate *Sarcinae* on the other side of the groin.

DR. BECKER: I think the lesion falls in the class of neurodermatitis. I did not see a great deal of scaling. The patient is overambitious. He worked during his vacation while going to college, and stated that he worked harder than any one else in his organization. In this class of patients one finds signs of deficient energy in the form of low basal rate and of low blood pressure. Some of the patients have responded well to a new extract of the suprarenal gland.

DR. FINNERUD: I would suggest that a Waelsch stain be made of the scrapings, which would demonstrate easily the presence of *Microsporon minutissimum*.

DR. MITCHELL: I have failed completely several times on neurodermatitis, and later have found fungi the presence of which I did not even suspect at first. Positive cultures and complete cure with chrysarobin in traumaticin demonstrate that the dermatoses were not neurodermatitis. It is easy to overlook a fungus infection of this type.

DR. OLIVER: The patient was shown just as a curiosity. I think Dr. White's suggestion of transferring the organism to the other side of the groin is good, and I shall do it.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

A traveling salesman, aged 35, had a number of lesions of the neurofibromatosis type, and in addition there was a peculiar wavy appearance of the skin over the trunk, due to numerous small areas of slight bulging of the skin.

DISCUSSION

DR. MCEWEN: I think it is interesting that this condition should be associated with vitiligo.

DR. ORMSBY: I think this is an important case, for the patient undoubtedly has symptoms of neurofibromatosis, and also of multiple, benign tumor-like, new growths. Such being the case, it would place the latter disease in the category of the former, which helps us out etiologically in placing that disorder. This adds to other evidence which promised that development.

DR. MITCHELL: Recently I saw a young woman who was one of eight children. Her father has the disorder to a marked degree, and so has she. She is below par mentally, but the other children are of average mentality, and are free from the disorder.

DR. WIEDER: In view of the extensive nature of the lesions I think it might be wise to have a roentgen study made of the bones.

DR. SENEAR: The peculiar, wavy appearance of the skin I took to be due to the change in some of the structures, probably of the elastic tissue. Several biopsies were done at the university, and I shall try to present the pathologic tissue. The particular thing I had in mind was what Dr. Ormsby has already brought out, that this case adds to the evidence that multiple, tumor-like, new growths are in reality a variety of neurofibromatosis.

PITYRIASIS ROSEA IN A CHILD. Presented by DR. FINNERUD.

A girl, aged 5, had an eruption of the trunk and extremities of four days' duration. The largest lesion was in the lumbar region, and preceded the general eruption by about one week. There were no constitutional or subjective symptoms.

DISCUSSION

DR. MITCHELL: I have been struck by the fact that pityriasis rosea in children at this time is extraordinarily common. I saw a child recently with that condition

who was just 5 years old, and I saw two under 10 years and a number of adolescent age.

A Case for Diagnosis (Tertiary, Nodular Syphilid, Tuberculosis?). Presented by Dr. Zeisler.

A man, aged 42, had two annular lesions of fifteen years' duration, situated on the calf of one leg. Each lesion showed an atrophic center and a pigmented, nodular, linear border. There was no history of a chancre.

Biopsy showed a plasma cell perivascular infiltrate and giant cells.

DISCUSSION

Dr. Wile: This case bears a striking resemblance to that of a patient with lesions on the forehead who was presented by Dr. Ormsby. The microscopic picture shows a very superficial granuloma, and the marked pigmentary disturbance is not incompatible with a diagnosis of a late syphilid. There are, however, no discrete nodules; the lesions all seem to be coalescent. I was rather inclined to think it would be a tuberculosis, but the microscopic observations are not in accord with this diagnosis.

Dr. Mitchell: I should like to ask whether the duration of the large lesion is as long as the patient stated. He said it had been present as long as he could remember, and I wondered whether it had been a birthmark originally.

Dr. Becker: I should think the marked hyperpigmentation would be in favor of syphilis rather than tuberculosis.

Dr. Zeisler: I first thought of syphilis, then granuloma annulare and possibly leprosy. I did not think of tuberculosis, and cannot conceive of tuberculosis, if it is hematogenous in origin, being localized in only one leg. It would be unusual to have tuberculosis of an annular type. As regards the histology, it is questionable whether it bears more resemblance to syphilis than to tuberculosis. The infiltrate is more perivascular, and the giant cells less typical than those usually found in tuberculosis. I would be inclined to diagnose the condition tertiary syphilis in spite of the negative reaction to the Wassermann and the Kahn tests.

Dr. Ormsby: It would be a most extraordinary thing for syphilis to remain in the same location for so many years. I have never seen that occur in syphilis. As a rule late lesions undergo resolution in a particular area, and develop in new situations. This case resembles one I showed today. I believe that in this case tuberculosis will be demonstrated.

Dr. Wile: It is too vascular for tuberculosis. Instead of showing a necrosis of tuberculosis tissue it is viable, just as a syphilid would look.

Dr. Montgomery: A superficial glance at the sections from this case suggests a diagnosis of syphilis rather than of tuberculosis. I have, however, seen tuberculosis verrucosa cutis present a similar histopathologic picture composed essentially of perivascular plasma cell infiltrate without any evidence of tubercle formation. In view of the histologic observations, together with the clinical picture, I would favor a diagnosis of tuberculosis.

Dermatitis Medicamentosa (Phenolphthalein). Presented by Dr. C. White.

An American housewife, aged 31, was first seen about two months previous to presentation when she complained of brown areas on her arms and legs of ten months' duration. These areas had appeared first as "red itching spots" on the back of the hands which later involved all extremities, as well as the upper part of the trunk. The areas gradually became brown; some would disappear and then return. She had taken many different kinds of pills for constipation. Her general health was excellent.

Physical examination revealed symmetrical, circumscribed, brownish areas which varied from ½ to 1½ inches in diameter, and were on all extremities as well

as on the chest and back. General examination gave negative results. The clinical diagnosis was made of a phenolphthalein eruption, or one due to an allied drug. Urinalysis was negative for all such drugs. A biopsy was taken because of the widespread pigmentation, but there were no observations of importance.

To make an absolute diagnosis, 1 grain (0.065 Gm.) of phenolphthalein (red) was given by mouth. One-half hour later she complained of marked itching in the old involved areas, and erythematous macules were beginning to appear in the same. One hour after ingestion these lesions were prominent as erythematous edematous macules, and the urine showed a positive reaction for phenolphthalein. These manifestations and observations confirmed the original diagnosis, and the case was presented because of such widespread involvement.

DISCUSSION

DR. OLIVER: I think Dr. White should be congratulated for his able presentation of an interesting case.

DR. FOERSTER: When this case was shown it recalled to mind a case that the late Dr. Fred Harris exhibited before the society a number of times with a condition diagnosed as erythema perstans, which later proved to be a phenolphthalein eruption. That patient had as many lesions as this on the extremities, and a great many on the back. In the course of a year or more during which time the patient was repeatedly shown before the society, we had an opportunity of seeing the pigmentation develop until it became almost black. I think that was the first case of phenolphthalein eruption observed in Chicago.

DR. MITCHELL: Dr. Ormsby and I observed a patient with a fixed exanthem at frequent intervals several years ago. Photographs were made, and all the recurrent lesions could be identified by the photographs. The eruption was of the phenolphthalein type, but it was evidently a multiform erythema in which phenolphthalein had nothing to do with the lesions. We tested him out repeatedly with all the drugs known to produce the eruption, but he reacted to none of them.

DR. WHITE: When I first saw this patient I thought of the persistent pigmentation of erythema multiforme, but clinically the case was considered a phenolphthalein eruption, which was confirmed by administration of this medicament.

TINEA UNGUIUM, FOLLOWING TRAUMA. Presented by DR. ZEISLER.

A woman, aged 30, received an injury to one hand six months before presentation. Since then the nails had come brittle and broke off easily at the distal margin. All the nails of the injured hand were involved, while those of the other hand were normal. Scrapings showed mycelial threads.

DISCUSSION

DR. MCEWEN: I believe it will finally be proved that this is a fungus infection.

D. SENEAR: That was my idea.

DR. LIEBERTHAL: I think it would be well to study the nails after removal of the beautifying varnish. The case impresses me as psoriasis of the nails. We have a duplicate case under observation. The patient in that case has only one other lesion, that is on the glans penis, and the lesions have been present for four or five years. In our case the lesions are bilateral.

DR. WHITE: We had a patient at the Northwestern University clinic not long ago whose condition closely resembled that of this woman. We looked for fungi and found them; the fungi were thin, long and narrow.

DR. MITCHELL: I have been particularly interested in this type of undermining, without loss of luster in ringworm of the nails. It so happens that in several such cases with separation of the nail from its bed, it was interesting to find that fungi were present and viable.

PITYRIASIS LICHENOIDES CHRONICA. Presented by DR. FOERSTER and DR. WIEDER.

A white woman, aged 26, single, a physician's attendant, suddenly developed a generalized eruption in the manner of an exanthem twenty months before presentation. The eruption has persisted since then with variable activity and without subjective symptoms or evidence of involution. Roentgenotherapy and other measures had been ineffectual. Her history otherwise was unimportant.

Examination showed a generalized, dully inflammatory eruption involving the trunk, extremities and neck, of uniform distribution. The lesions were slightly infiltrated and inflammatory papules varying in size from that of a grain of rice to that of a small pea, most of which were surmounted by thin, adherent scales, made more apparent on scratching. Physical examination otherwise was negative.

The patient had received a fractional dose of roentgen rays to the area of the thymus gland six weeks before presentation, which had been without apparent effect. She was presented for therapeutic suggestions.

DISCUSSION

DR. ORMSBY: I should like to inquire whether the patient improved under the treatment that was suggested.

DR. FOERSTER: There was no improvement.

DR. MCEWEN: I was under the impression that hyperthyroidism was present; there was some exophthalmos and a rather rapid pulse. She had an infection in her mouth also, and any attempt at therapy should include cleaning up of all infection.

DR. WIEDER: The patient was presented chiefly for suggestions for therapy. In addition to the roentgenotherapy we have treated her with zinc peroxide ointment, but without effect on the lesions.

DR. ORMSBY: It might be that some benefit would be derived from treatment with the quartz light. We have had one patient with the lichenoid type of lesions whose condition cleared up under treatment with neoarsphenamine, and another whose condition cleared up while he was under treatment with neorobin. The one treated with neoarsphenamine had no recurrence, but the disorder recurred in the one treated with neorobin. In the Brocq type our results were negative until we used the quartz light. That was used at the suggestion of Chipman, who cleared up all types with it.

DR. LIEBERTHAL: I would suggest that you increase the strength of the zinc peroxide ointment to 10 per cent.

DR. SENEAR: I should like to know whether any of the members have had any experience with the treatment of patients with this disease with calcium lactate. I had good results in a case of the pityriasis lichenoides chronica type, with no other therapy. The patient is practically free from the eruption, and there is no sign of a recurrence. I gave a dose of 5 Gm. of calcium lactate morning and night.

DR. FOERSTER: I presented a young Italian laborer before this society, in 1915, who had a similar and more widespread eruption. Shortly afterward he was recalled to join the Italian army and spent much of his time in a part of Italy where there were radio-active waters, in which he bathed regularly. When he returned to this country he was completely cleared of his pityriasis lichenoides chronica, and there had been no recurrence when he was examined last, about three years ago.

DR. FINNERUD: I saw a case of this disorder with Dr. Oppenheim which was cleared up with tuberculin therapy.

DR. WILE: I wonder whether occasionally some of these patients get well spontaneously. I have seen a patient who got well spontaneously after an erythroderme en placques. Some of them I think are benefited by sulphur baths.

If they respond in isolated instances to such varied types of therapy, it may well be that they clear up spontaneously on some occasions.

ATROPHY OF FACE (ROENTGEN RAY). Presented by DR. RUBEN NOMLAND.

A woman, aged 28, had been treated by the Tricho-System for superfluous hair on the face about twenty-four months before presentation. She received ten treatments to each of four areas on the face, at intervals of about two weeks. Twelve months ago she noted that the skin of her face was dry and scaly, and had recently noted a "spot" on her chin. At no time had there been acute dermatitis.

Examination showed that the skin that covered the chin, upper lip and sides of the face was dry and slightly scaling. There was a definite fine wrinkling due to atrophy. The superfluous hairs had disappeared. In the left submental region was a telangiectatic area about 1 cm. in diameter.

DISCUSSION

DR. MCEWEN: This is an interesting case, and I think that two or three years from now her face will look worse than it does at present.

DR. LIEBERTHAL: I think the whole thing is exceedingly pitiful. We all see patients of this type, and explain to them that we have proof that the roentgen ray for permanent epilation is followed by disastrous results, but we are not able to dissuade them from going to these places.

DR. FOERSTER: I think it is known to all dermatologists that the Tricho-System employs the roentgen ray, though this fact is apparently not understood by health officers, other physicians or the public. I examined one of their machines, the use of which had been responsible for a severe radio dermatitis, and saw a roentgen tube inside the apparatus and obtained a roentgenogram while the operator demonstrated the apparatus.

DR. ZEISLER: I should like to know how severe the hypertrichosis was before treatment. It seemed to me to be a good result so far as the removal of the hairs is concerned.

SCLERODACTYLIA WITH CALCIFICATION. Presented by DR. RUBEN NOMLAND.

A Jewess, aged 58, was first presented at the annual meeting of the Chicago Dermatological Society, by Dr. Ebert and Dr. Ormsby, in 1925, and the history of the case is recorded in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY **12**:409, 1925.

The patient first noticed stiffening of the forefinger of the right hand in 1918, and in the course of two years all the fingers were involved. About 1923, she first noted thickening of the skin over the upper part of the right side of the chest and clavicular region, which had now disappeared. Acrocyanosis and symptoms suggestive of Raynaud's disease had been present since soon after the onset of the disorder, and a periarterial sympathectomy was performed on the right side in 1925, without improvement. The condition had remained stationary for the past several years, in spite of much and varied therapy. Since 1923, there had been recurrent necrosis of the skin over the deposits of calcium present in the fingers, with repeated abscess formation and extrusion of the calcium deposits.

Examination showed a small, slight, "dried up" woman, who appeared much older than her stated age. Aside from the skin disorder general examination revealed little. She gave a history of gastro-intestinal trouble that had been diagnosed as cardiospasm. The fingers were short, stubby and stiff, and the distal phalanx in several instances had disappeared. The nails showed marked trophic changes. The palmar aspect of the fingertips was the site of numerous, small, pitted scars. On the left third finger was an area of acute inflammation, in the center of which was a white particle of calcium, 1 mm. in diameter, just beneath

the epidermis. Over the upper part of the right side of the chest and clavicle was a patch of atrophic, slightly depigmented skin.

The Wassermann reaction of the blood and the urinalysis were both negative. A roentgenogram of the chest revealed no abnormal conditions; but one of the stomach showed dilatation of the esophagus which suggested cardiospasm. A recent roentgenogram of the hands revealed calcium deposits in the tips of all fingers, most marked in the thumbs and on the third finger of the right hand. The distal portion of the third phalanx had been destroyed in nearly all the fingers. There was no evidence of arthritis.

DISCUSSION

DR. ZEISLER: This is an interesting and unusual case. I remarked that we do not see many such cases, but Dr. Wile said that he sees quite a number.

DR. WILE: The most interesting feature of this case to me is in the calcified material cast off from various lesions. Calcification in connection with sclerodactylia is, I believe, common enough, but its extrusion through the skin is, I believe, rare. At least, I have never seen the condition occur in just this way.

DR. EBERT: I presented this patient some years ago at the annual meeting of the society, and have been interested in this type of case. On looking over the literature I find that this particular type is rare. There are a few cases in the French literature. I had an opportunity to see at the Presbyterian Hospital a patient with sclerodactylia and exactly the same type of lesions that this woman shows, with the deposits of calcium that form sterile abscesses, and later slough out. She also had Raynaud's disease which affected the cerebral vessels. I also saw a case almost exactly like this in Paris.

DR. MITCHELL: Has any one tried a completely calcium-free diet with the injection of parathyroid hormone? The idea is to make the parathyroid hormone mobilize these calcium deposits.

DR. ORMSBY: I have seen calcium deposits in patients with sclerodactylia but not in the fingers. In a case I have in mind the deposits were about the elbows. There was some localized scleroderma about the elbows in this case, but the fingers were chiefly affected. This patient was thought to have Raynaud's disease, but we later decided that it was sclerodactylia.

DR. NOMLAND: The particular thing of interest is the fact that the scleroderma has largely cleared up, while the condition of the hands has steadily become worse. I had occasion to look up a report on a series of fifty cases of scleroderma from the Mayo Clinic, and only two of the fifty had calcification. Neither case was similar to this one.

DR. ORMSBY: Another point of importance is that the periarterial sympathectomy on the right arm was without any effect on the process in that hand.

DR. MONTGOMERY: The absence of beneficial effect from the sympathectomy is of interest in this case. At the Mayo Clinic, Dr. O'Leary, Dr. Brown and Dr. Adson have been especially interested in these cases, and they recently observed two cases of sclerodactylia without deposits of calcium, in which marked beneficial effect was seen following sympathectomy. I recently saw a case that was almost a duplicate of the case under discussion. The patient had prodromal symptoms of Raynaud's disease, and presented a marked sclerodactylia. There were definite calcium deposits being extruded from the fingertips. It is planned to do a sympathectomy, and the results will be reported later.

DR. NOMLAND: In 1925, Dr. O'Leary and Dr. Brown reported a series of cases of sclerodactylia-like lesions in Raynaud's disease, some cases of true sclerodactylia and others of pseudosclerodactylia.

DR. BECKER: These cases, I think, are not uncommon, but they are seen by the internists and neurologists rather than the dermatologists. We have a patient whose symptoms started as those of Raynaud's disease in the middle fingers on each hand, and now she has typical scleroderma. In another case demonstrated as Addison's disease there were typical addisonian symptoms, and the clinicians had missed the sclerodactylia with the terminal scars this patient has.

MELANOTIC SARCOMA. Presented by DR. E. P. LIEBERTHAL.

A woman, aged 45, presented a crescent-shaped, bluish-black, elevated lesion on the dorsum of the left foot. The crescentic shape was due to the cauterization of the lesion which had been performed by her family physician eight months before presentation. The condition began one and one-half years before presentation as a bluish-black, elevated lesion the size of a pea. Following the application of a corn cure by the patient one year ago, enlargement rapidly took place until the present size was attained.

DISCUSSION

DR. WILE: I think we are all inclined to regard these cases as hopeless. During the last year I have heard of one patient who completely recovered after the removal of a large, rapidly growing melanotic tumor, in which there could be no question of a malignancy. I think ninety-nine of one hundred patients will die, but here is a woman with a small lesion, and with no evidence of deep fixation or metastases, and it seems to me that with a full understanding of the small chance she has, the lesion should be widely excised.

DR. MONTGOMERY: I wish to emphasize what Dr. Wile has said. In regard to the histopathology, Broders has clearly pointed out that the more pigmented (blacker) the tumor is, the relatively less malignant it is. In other words one of the functions of the cells of a tumor in melano-epithelioma is to form pigment. Therefore, the cells that show ability to do this are more highly differentiated and consequently the tumor which is capable of forming pigment is less malignant than one which is not. The clinical appearance, however, depends on other factors than merely the melanin content of the tumor. I know of one case in which a melanoma was excised fourteen years ago with no evidence of recurrence as yet.

DR. ORMSBY: I have seen two lesions of this type about the eye and several in other locations which have been treated successfully with roentgen rays. On the other hand, I have seen patients who have died following surgical excision of the primary lesion. Several others have not progressed. I believe that there is no question but some of them are benign, and I agree with Dr. Wile that we should not view them as absolutely hopeless. Some patients do recover. I have observed several patients over a period of years following treatment, who have had no recurrence.

DR. WHITE: When I was at the University of Pennsylvania I gained the impression at various dermatologic meetings that the darker the lesion, the more malignant it was. I would like to hear what the general opinion is. It seems to me that no positive statement can be made on the pathogenicity of the pigmentary content of a nevus without histologic study.

DR. ORMSBY: Those I have seen have been bluish-black, not jet black as the lesion in this case is. I saw a bluish-black lesion in the eyebrow and suggested that it be not treated. About two months afterward a surgeon notified me that he was going to remove it, and asked me to be present at the operation. He made a complete excision of the lesion as examination of the sections later showed. Notwithstanding, general metastatic involvement occurred which induced a fatal termination within fifteen months.

DR. WILE: I have seen original lesions with practically no color in which the metastases have all been pigmented.

DR. BECKER: The lesion from which the malignant melanoma develops is usually light brown. The dark moles which have persisted for many years are generally not so apt to develop into malignant lesions. The blue-black lesions are already malignant, and the difference in color depends on the pigment content and the depth of the lesion in the skin.

DR. LIEBERTHAL: The interesting thing in this case is the fact that deep cauterization of the lesion by the family physician two years ago did not result in local proliferation nor in metastases, thus speaking for a low grade malignancy.

A Case for Diagnosis. Presented by Dr. Senear and Dr. Wien.

A woman, aged 38, first noted some red spots on her feet in December, 1928. She had a cold in the head, and had taken six quinine capsules within the two days that preceded the appearance of the spots. Pain in the joints was also noted at the time of appearance of the eruption of the feet. Since that time she had had successive crops of red spots on both legs, thighs and arms, the crops appeared at intervals of from seven to fourteen days, and each new lesion appeared slightly elevated. Her general health had always been good. She had taken various medicines prescribed for her since the onset, but there had been no internal medication during the past three weeks. In January, 1929, she applied heat to some of the areas on the legs, and subsequently noted blisters, then crusting and infection.

Examination showed diffuse involvement of the extremities with purpuric papules which varied in size from that of a pinhead to that of a pea. The lesions were in various stages of involution; some were recent and others presented the changes of old lesions. Both lower extremities presented scattered lesions of an involuting ecthyma. The Wassermann reaction of the blood was negative. Blood chemistry values were within normal limits, the cholesterol being slightly increased, 217 mg. per hundred cubic centimeters. The blood picture showed 94 per cent hemoglobin, 4,720,000 red blood cells; 7,040 white blood cells; 22 per cent large lymphocytes, 18 per cent small lymphocytes, 2 per cent mononuclears, 56 per cent polymorphonuclears and 2 per cent eosinophils.

DISCUSSION

Dr. Wile: I think this patient had two, or possibly three conditions. First, a definite purpura on the thigh. The lesions on the arm were yellowish, slightly resembling xanthomas, but I think they were of the urticarial type. What she had on her legs I think was the result of infection.

Dr. Zeisler: I think the patient has xanthomatosis. Possibly the lesions on the extremities might have been induced by the bromide she was taking.

Dr. Foerster: I think the lesions also have an urticarical character, and I believe that there is a uniform etiology for the whole dermatologic condition. She must have a focus of infection somewhere from which she derived toxin.

Dr. Senear: My idea was that expressed by Dr. Foerster. The patient has two conditions, an ecthyma which is secondary. I have watched her in the hospital for several weeks, and have seen her develop three showers of the lesions she now presents. In each instance involution started in a few days and we thought of sending her out, but the next day we would find she had developed a new crop.

The eruption started in December with a distinct eruption of the legs, a condition more purpuric than that today, and following that was the appearance of the nodular element, probably urticarial in type.

Scleroderma. Presented by Dr. Oliver and Dr. Finnerud.

A man, aged 36, complained of sensations of stiffness, drawing and burning of the skin, chiefly of the extremities and face, of eight months' duration. He had had no treatment. The basal metabolic rate was + 3.

Examination showed that the skin of these areas was diffusely glistening and tense, of waxy and leathery character, and that its normal lines were obliterated. In places atrophy was distinct.

A Case for Diagnosis (Tuberculosis?). Presented by Dr. Ebert.

A woman, aged 30, injured the elbow of her right arm five months before presentation and developed a secondary infection in the area which did not heal. It slowly spread, and always seemed moistened with pus. Six weeks ago a new area developed just above the elbow. There was no history of trauma in this instance, and the lesions had never been painful.

The patient gave no personal or family history suggestive of tuberculosis. She had been married for twelve years, had four children living and well, and had

one miscarriage between the last two normal deliveries. When she first appeared in the clinic one month ago, the lesion on the elbow was raised, papillomatous and bathed in pus, the base of the lesion appeared much the same as at the present time. Although the Wassermann reaction of the blood was negative both before and after treatment, she was given four injections of neoarsphenamine at approximately weekly intervals. The lesions had improved, but had not healed.

The intracutaneous injection of 0.2 cc. of a 1:10,000 Koch's old tuberculin gave a negative reaction, but the intracutaneous injection of 1:1,000 Koch's old tuberculin gave a positive reaction. The pus from the margin of the lesion was examined for organisms of blastomycosis, but none were found.

On the right elbow there was a bluish red, slightly raised, moderately infiltrated plaque the size of a quarter, somewhat scaly in the center, and there were two shallow ulcers the size of split peas covered by crusts which discharged seropus when the crusts were removed. About 2 inches higher was a similar plaque the size of a dime, covered with coarse scales.

DISCUSSION

DR. WILE: The lesion looked to me like an involuting blastomycosis.

DR. NOMLAND: The section shows practically a pure plasma cell infiltration of the cutis; I think there are no blastomycetes in the section. There is no tubercular structure, and it is a localized nonspecific granuloma.

DR. EBERT: One of the first things we thought of was blastomycosis, and we searched carefully for the organism. We found nothing that resembled this. The abscesses were not typical, and the microscopic evidence was not of that disorder. She has had four injections of arsphenamine, which cleared up the papillomatous element. The bluish border suggested tuberculosis to me.

BLASTOMYCOSIS CUTIS (CARCINOMA?). Presented by DR. SENEAR and DR. CORNBLEET.

A white man, aged 70, entered the clinic two weeks before presentation complaining of a condition of the face, neck and tongue. This commenced a year and a half before presentation as a small nodule under the left side of the mandible, and soon afterward was followed by a second nodule under the right side of the mandible. These enlarged slowly for seven months to form painless, nontender, subcutaneous masses the size of a hen's egg. At that time, two nodules appeared one on each cheek, which in a month grew to the size of a walnut, and pointed through the skin. Since then other nodules had appeared, and followed the course of the latter two. Three months after the inframandibular lesions appeared, the posterior portion of the tongue became sore, and this feeling had slowly changed to one of relative immobility.

At the time of presentation there were subcutaneous nodes and nodules on the face and neck over some of which the skin was freely movable, and over others it was attached. Some were in different stages of pointing through the skin, and from these a scanty, thin pus could be expressed. All the lesions were infiltrated, and in most places had become woodlike. The tongue, except for a thin shell at the sides and tip was a mass of infiltration, and was neither painful nor tender.

The course of the disease had been in cycles of three or four weeks, at the beginning of which new lesions appeared, and older ones became activated; in the interim, all lesions regressed and became relatively quiescent. The lesions appeared as small nodules subcutaneously, enlarged, attached themselves to the skin, which then took on a sluggish purple hue followed by the forming of sinuses, discharged a small amount of pus, and healed with a puckered scar. The woody hardness came on slowly during the entire process.

A section from a biopsy of a young lesion showed that the epidermis was intact with edema of the layer of the basal cell. The papillae were flattened and hyalinized connective tissue, lymphocytes, polymorphonuclears and plasma cells, and occasionally foreign body giant cells were interspersed.

Examination of the blood showed 4,280,000 red cells and 8,850 white cells, the hemoglobin was 70 per cent; differential white count showed polymorphonuclears 80 per cent, large mononuclears 3.5 per cent, lymphocytes 13 per cent, eosinophils 2.5 per cent and basophils 4 per cent.

The Wassermann and Kahn tests on the blood both gave negative reaction.

NOTE.—For two weeks following presentation during which there had been no specific treatment, improvement was observed in all the active lesions without the appearance of any new ones.

Direct smears from four different lesions as well as from a puncture of the base of the tongue showed nothing but large blastomyces-like yeast cells. Since then, however, the active lesions had been regressing, the pus had been scanty and difficult to collect, and this had shown neither the previously found nor any other organism. The organisms were found abundantly both by the ordinary preparation of potassium hydroxide and by special staining method. Cultures were too young to be useful.

DISCUSSION

DR. BECKER: I think this is probably some sort of mycotic infection. The histologic picture is that of a granuloma such as we might find in blastomycosis or any of the related conditions. I do not wish to make a definite diagnosis.

DR. WHITE: Clinically I would call it a deep fungus infection, but microscopically it is not one of the ordinary ones.

DR. SENEAR: When we first saw this man we were much at sea. We thought of the possibility of carcinoma, with the relation of the tongue and submaxillary condition, but could not reconcile the lesions on the cheeks with this, if that was part of the same process. Then the double contoured organism was recovered from the lesions on the tongue and cheek. Our feeling before the discovery of the fungus had been that expressed by Dr. Becker, that it would prove to be a mycotic infection of some sort. The cultures have not yet matured, and I have no idea as to whether this is actually the pathogenic factor.

DR. WILE: Is it common to find a degree of glandular involvement that is so hard as in this case? The massing of the glands and the extreme induration is not the type one should ordinarily expect from mycotic infections such as occur in sporotrichosis or other mycotic infections, but suggest to me rather malignant metastasis.

DR. SENEAR: We have never seen anything like the induration present in the glands and submaxillary region, and it was this that brought up the possibility that there were two distinct conditions in the case.

DR. FOERSTER: I see no reason why this patient cannot have carcinoma as well as blastomycosis. I recall the case of a patient with ulcerative and nodular lesions on the neck from which I obtained pure cultures of sporothrix on several different occasions at intervals of more than a month, both from the ulcer and from associated cutaneous abscesses. A histologic diagnosis of epithelioma was subsequently made on the margin of the ulcer, and the case was apparently one in which both diseases existed. We had an elderly man under observation recently who had ulcerative and infiltrative lesions of the mouth, neck and chest with deep involvement and multiple sinuses, suggestive of either actinomycosis or blastomycosis. At autopsy a diagnosis of carcinoma was made, though that disease was not apparent clinically.

DR. CORNBLEET: I made a deep stab wound and found the same organism that we found in the pus.

A CASE FOR DIAGNOSIS. Presented by DR. FINNERUD and DR. OLIVER.

A negress, aged 40, complained of a patchy darkening of the skin of the face, neck and upper extremities of six months' duration. There were no subjective symptoms. The condition had partially disappeared on the forearms, where it began. Her occupation for the past six years had been that of polishing silver

and scrubbing floors for the Pullman company. She had had no previous skin disease, and had taken no medicine except compound cathartic pills and quinine.

Examination revealed hyperpigmentation in patches varying in size from that of a coin to that of a palm; the individual patches were of lichen planus-like outline. There was no infiltration or atrophy perceptible. The mouth was in a grossly normal condition.

Histologic sections showed no noteworthy changes except numerous large chromatophores in the papillary portion of the corium.

DISCUSSION

DR. OLIVER: We first saw this patient at the clinic two weeks before presentation, and have not yet reached any definite conclusion as to what the condition may be.

DR. BECKER: There is an enormous number of pigment cells beneath the epidermis. They are not so deep as one sometimes finds them, but the nature of the cells suggests that they are of the type found in a blue nevus. It may be that in the colored race the phagocytic cells have this appearance.

DR. FINNERUD: This patient has not yet been examined from a general medical standpoint. One of the interesting features is that all of the patches with the exception of those on the face and lower portion of the forearm have much the outlines of those of lichen planus. However, the pigmented areas are without infiltration or atrophy, and the patient states that they have never been of other than the present appearance. The histologic picture is interesting, the increase of pigment was apparently limited to the papillary layer of the corium, and there was practically no evidence of inflammatory change.

FOLLICULIS, ACNE VULGARIS. Presented by DR. CLEVELAND WHITE.

An American negro, laborer, aged 27, had had an eruption on his face for many years, but in the past six months there had appeared papules and nodules on the dorsa of the hands, extensors of the forearms and on the lower part of the abdomen; none was accompanied by any subjective symptoms. Four years previously he had a bilateral cervical tuberculous adenitis, the involved glands of which had been surgically removed, and the pathologic observations were typical tuberculosis (Dr. T. K. Lawless). His general health was good except for some pain in both feet due to calcaneal spurs (orthopedic Department of Northwestern University Medical School).

Examination revealed many comedones, papulopustules, cysts and irregular scars on the face. On the extensor surfaces of the forearms and hands were many firm, discrete, elevated nodules varying in size from that of a pea to that of a hazelnut. Many of these nodules were follicular, and some small dark colored hyperkeratotic follicular centers resembled comedones on a cursory examination, but further study suggested a different process. On the proximal areas of the forearms near the elbows were many round, somewhat depressed scars from 0.3 to 0.5 cm. in diameter. The lower part of the abdomen presented many papules and nodules similar to those on the forearms, but the black follicular centers closely resembled comedones. Sections of tissue were taken from the face, abdomen, extensor surface of the left forearm and from the dorsum of the left hand. Study of these showed the usual acne vulgaris observations on the face, and practically the same on the abdomen. The biopsies from the hand and from the forearm were considered actual tuberculosis; further sections were to be taken from the abdomen, for it was still felt that a tuberculous factor might be present.

The roentgenogram of the chest was interpreted by Dr. W. T. Bronson as showing no active tuberculosis, but it revealed the presence of some scar formation in both apexes. The Wassermann reaction on the blood was negative; the blood and differential counts were normal and urinalysis gave negative results.

The case was presented because the lesions on the hands and forearms were clinically tuberculids and so widespread.

MINNESOTA DERMATOLOGICAL ASSOCIATION

June 22, 1929

W. H. GOECKERMAN, M.D., *President*

DERMATITIS-HERPETIFORMIS (?) PEMPHIGUS (?).

All cases at this meeting were presented by Drs. O'Leary, Goeckerman, Montgomery and Brunsting.

A man, aged 53, had been married for twenty-seven years and had ten children living and well. He had been well until the onset of his present illness, nine or ten years before presentation. On admission to the hospital, the lesions were on the scalp, face and extremities, and to a slight degree on the trunk. The elementary lesion was a vesicle, and later, bullae, with surrounding erythemia, and crusted and excoriated lesions developed. Some of the vesicles had become infected. The patient complained of burning and itching. The history of definite periods of remission was elicited.

When he was first seen on April 5, 1929, a diagnosis of seborrheic dermatitis was made. There was much scaling and crusting about the scalp and ears. There were also crusting, scaling and a few pustules about the neck, axillae, groins and abdomen. In the hospital numerous vesicles with erythematous bases developed over the spinal column, groins, axillae and shins. The diagnosis then changed to probable dermatitis herpetiformis. On April 11, following a paravertebral treatment with roentgen ray, there was much improvement in the condition over the back. The report of biopsy was indeterminate.

DISCUSSION

DR. SWEITZER: I thought that the patient had seborrhea of the scalp. There is a question of pyogenic infection or dermatitis herpetiformis on the legs. With no evidence of itching on the legs, I believe that the condition is pyogenic.

DR. O'LEARY: The patient has presented, at various times, a fairly typical picture of dermatitis herpetiformis. On occasions, also, there have been features suggesting pemphigus. At the present time the acute exacerbation is the result of a flareup, following the administration of potassium iodide. The case is an example of the borderline type of dermatitis herpetiformis and pemphigus, but has not shown any of the features of erythema multiforme which are also associated with the combination.

DR. BOREEN: The situation of the lesions on areas except the legs is typical of seborrhea. The diagnosis rests between dermatitis herpetiformis and pemphigus. I should favor a diagnosis of benign pemphigus.

DR. MICHELSON: I think that the man has dermatitis herpetiformis, but if there is some doubt the iodide test might be applied. In Bern, Professor Naegli also used iodide therapeutically. He begins with a minimum dose, gradually increasing it until there is a definite reaction, and then he begins again with a small dose after the reaction subsides.

PAPULONECROTIC TUBERCULIDS. ERYTHEMA INDURATUM. LUPUS PERNIO. ACROCYANOSIS.

A mail carrier, aged 30, married, presented the following family history. His mother was living but had gallbladder trouble. The father was dead; he had had Bright's disease. Two sisters were living and well. At the age of 15 nodules had developed on the legs which had ulcerated and left scars. Since then he had had recurrence of the lesions off and on. Six or seven years before presentation similar ulcerating lesions had appeared on the toes of both feet. He had also had recurrent iritis for the past fifteen years, and swelling of the glands of the neck at that time.

Examination of the urine revealed red blood cells and pus. The blood count was normal, and the Wassermann reaction of the blood was negative. Ocular

examination showed evidence of old iritis. Roentgenograms of the thorax revealed evidence of old tuberculosis of the upper lobe of the right lung and old pleuritic adhesions of the right costophrenic angle. Roentgenograms of the vessels of the leg gave negative results.

DISCUSSION

DR. GOECKERMAN: We often see acrocyanosis in association with tuberculosis here in the clinic.

DR. MICHELSON: This patient presents a rather complex picture. Undoubtedly, the cervical adenitis, the scars on the arms and legs and the roentgenographic evidence are positive for tuberculosis. I cannot conceive of the ulcers on the toes being tuberculous in origin. The patient says that he has been a heavy cigaret smoker since early youth, and the possibility of a nicotine ulcer should be considered. Tobacco may be a factor in the acrocyanosis, and the ulcers may be traumatic in origin.

DR. BRUNSTING: This case demonstrates the varieties of tuberculosis that one patient may present, and at the same time emphasizes the influence of resistance in altering the clinical picture. The patient was admitted yesterday; hence the reports of biopsy are not available.

FOREIGN BODY REACTION.

A woman, aged 51, a native of Alaska, had been under treatment for diabetes insipidus and for neurosyphilis. The upper part of each arm was covered with large, depressed, atrophic plaques. Practically no discoloration was noted. At one time she had treated herself with surgical solution of pituitary hypodermically, making the injections into her arm. The microscopic picture showed, essentially, fibrosis with hemorrhage and early foreign body reaction similar to that seen in tache bleuâtre of morphine addicts.

TUBERCULOSIS VERSUS SYPHILIS.

A woman, aged 54, came under our care in 1918, when latent syphilis was recognized and treated with three courses of arsphenamine and mercury. At the end of this time the Wassermann reaction of the blood was negative. In August, 1928, she complained of a tired feeling and listlessness. In October, the glands in her neck enlarged and were drained surgically several times. In March, 1929, a tender tumor developed in the presternal region, and in May the right axillary glands were recognized as being enlarged.

Examination revealed normal urine and a normal blood count. Roentgenologic examination of the thorax gave negative results. Several times the Kolmer modification of the Wassermann reaction of the blood was negative; all Kahn tests were positive, from +++ to ++++. One week prior to presentation the patient was given a therapeutic test, consisting of mercury and potassium iodide; purposely, the use of arsphenamine was avoided.

DISCUSSION

DR. REUTER: It is our impression that the present lesions are tuberculous and not syphilitic. The positive Kahn test may be a nonsyphilitic reaction or may be authentic, as we know that the patient has had syphilis. Further observation is necessary.

SOLID EDEMA OF THE FACE (LOCALIZED MYXEDEMA).

A woman, aged 32, married, who had two children, reported that for the last nine months she had had a swelling of the face, at first transient, but recently permanent. The swelling had flared up, especially under emotional excitement and strain, although there was no history of associated chills or fever. The edema was

of the nonpitting type and was most marked on the cheeks. The remainder of her skin showed no abnormalities. Septic tonsils and two periapically abscessed teeth were found. On admission, the basal metabolic rate was —12 and —13. On June 11, 1929, the basal metabolic rate was —6 after two weeks of desiccated thyroid gland therapy.

DISCUSSION

DR. O'LEARY: I presented this patient with the hope of arousing some discussion on localized myxedema of the face. The history does not elicit the onset of the swelling as following erysipelas or any intercurrent infection. There has been slow, gradual increase in the edema, with periods of remission. In a study of localized myxedema of the extremities following thyroidectomy for exophthalmic goiter, I was struck with the frequency with which cases of myxedema have been reported confined solely to the face. In view of the lowered basal metabolic rate and the absence of other explainable evidence to account for the edema, I have tentatively placed her in the group of localized myxedema.

SUBSEQUENT NOTE: After a two months' use of desiccated thyroid gland, 1½ grains (0.097 Gm.) daily, the edema has entirely subsided, the basal metabolic rate has returned to plus 4 and general improvement has been rather marked.

RECURRENT ERYSIPELAS WITH LYMPHANGITIS AND EDEMA OF THE RIGHT ARM.

A man, aged 47, came to the clinic because of recurrent attacks of erysipelas and resulting lymphangitis and edema of the right arm. The trouble had started in 1913, when the patient had been bitten in the right thumb by a dog. He had had no difficulty then until 1914, when a sinus had appeared on the palmar surface over the right thumb. This had tended to heal and break down for a period of ten years. In 1924, it was thought that the sinus was syphilitic, although the Wassermann reaction of the blood was negative. He had been given some treatment, possibly antisyphilitic, and later on treatment by the roentgen ray and radium. In 1924, the first attack of erysipelas had developed. At the end of this attack it had been thought necessary to operate on the bone, and the bone had been scraped. This had been followed by recurrence of the swelling in three months. In January, 1927, he had the thumb amputated because it interfered with his work. In September, 1927, he had a recurrent attack of erysipelas; this disorder had recurred since at frequent intervals. Roentgenologic examination gave evidence of destructive arthritis of the elbow. He has been given typhoid vaccine and treatment with the roentgen ray. This case was presented for diagnosis.

Biopsy of the right palm showed inflammatory changes with marked involvement of the blood vessels; there was fibrosis. In one area a deposit of calcium was shown. The microscopic picture suggested elephantiasis of the dura.

DISCUSSION

DR. O'LEARY: In contrast to the preceding case, this patient demonstrates elephantiasis as the result of recurrent lymphangitis. The history of onset following a bite from a dog has lead to intensive search for some organism other than streptococci in an effort to explain the attacks. Examinations, however, have all been futile. He has received typhoid vaccine intravenously in conjunction with treatment with the roentgen ray, but the condition has improved only slightly. The question has arisen as to the advisability of performing a Kondoleon operation with the hope of reducing the edema, which, in itself, may be the factor predisposing him to the recurrent attacks of erysipelas. The surgeons are loath, however, to operate at this time because of the frequency with which the erysipelas has been appearing during the past few months.

DR. GOECKERMAN: This case is analogous to the type referred to as recurrent lymphangitis. The periodicity of attacks with spontaneous limitation, I think, speaks for this. The microscopic picture is also suggestive of this, and the condition has responded slightly to treatment with foreign protein. It is, however,

an unusually severe case and undoubtedly has features of cellulitis. The present enlargement, I think, is essentially elephantiasis, akin to elephantiasis nostros.

HYPERTROPHIC LICHEN PLANUS.

A married woman, aged 66, said that five years before admission she had had a generalized eruption which had been diagnosed as eczema. This had persisted for three or four months and then had disappeared. A year before admission a spot on the left ankle had reappeared and ten months later the existing eruption had developed. On the extensor surfaces of the forearms and legs there were hypertrophic lichenified plaques. On the wrists, and scattered about the plaques, were numerous flat topped polygonal papules. She had received much relief from mercury protiodide, 1/6 grain (0.01 Gm.), and one-half skin unit of roentgen rays. The biopsy was typical of lichen planus.

EPITHELIAL NEVUS.

A girl, aged 4 years, came under observation because of verrucous lesions and scaling plaques on the extensor surface of the left forearm, the buttocks and the vulva. The mother said that the lesions had been present since one month after birth. They had always been in the same areas and at times had been associated with considerable itching. General examination gave negative results. The result of the tuberculin test also was negative. Biopsy was shown.

DISCUSSION

DR. MICHELSON: Histologically, the diagnosis might well be epidermal type of nevus.

DR. MONTGOMERY: I felt that the microscopic picture presented practically all of the features described by Gans as belonging to the so-called epithelial nevus, in which no true nevus cells are present.

TINEA BARBAE.

A farmer, aged 23, said that three weeks before admission a small, raised, swollen area had appeared on the right cheek; later, small pustules had appeared. Similar lesions had appeared under the chin and on the cheeks. He said that his calves at home had "ringworms" around the eyes. The preparation in potassium hydroxide showed a large spored ectothrix.

MYCOSIS FUNGOIDES.

A man, aged 49, gave a history that at 12 years of age a lesion in the right groin had developed and that it had persisted. Twelve years later, at the age of 24, several lesions had appeared at the waist line and where the suspenders crossed the back. There had been marked increase in the number of lesions in the last five or six years. Examination revealed adenoma of the thyroid gland and diabetes mellitus. Thyroidectomy was done for multiple adenomas. Laboratory tests showed the hemoglobin to be 78 per cent; erythrocytes numbered 4,090,000 and leukocytes 8,900 in each cubic millimeter; the percentages of the various types of leukocytes were: lymphocytes 26, large mononuclears 3, transitionals 4, neutrophils 65.5 and eosinophils 1.5. Roentgenologic examination of the thorax gave evidence of infiltration of the cavity on the left. Metastasis was to be considered. The microscopic picture of a section from one of the infiltrated plaques showed the polymorphism of the infiltrate and epithelial changes seen in the early stages of mycosis fungoides.

DISCUSSION

DR. MICHELSON: It is to be noted that the lesions here are all oval or round. It has been observed, and confirmed, that the premycotic stage of mycosis fungoides almost always occurs as round lesions. Mycosis fungoides is not preceded by a linear form of dermatitis.

TERTIARY SYPHILIS, CUTANEOUS (HYPERTENSION).

A married man, aged 59, presented no history of syphilis. The lesion on his leg had begun six months prior to presentation as red nodules which had coalesced. At the time of examination, an indurated, rather deep ulcer, 7 cm. long and 5 cm. wide, was situated on the lower one third of the inner aspect of the right leg. A tendency for peripheral extension and healing of the center was noted. There were a few varicose veins on both legs. A scar following surgical incision that had been made three months previously was visible. The Wassermann reaction and Kahn test of the blood were positive. He had had hypertension for twenty years. The systolic blood pressure was 210 and the diastolic pressure 98, measured in millimeters of mercury.

TERTIARY SYPHILIS WITH INVOLVEMENT OF THE LIP.

A single man, aged 35, reported that a lesion had started on his nose seven months before admission, and that it had gradually involved the upper lip. At the time of examination the edema of the lip and nose surrounded a group of indurated nodules, some of which were excoriated and crusted. A few isolated pustules and papules surrounded the lesion. He had acquired a chancre in 1912, and at that time had received four injections of arsphenamine and forty-two mercury rubs.

INFECTIOUS ECZEMATOID DERMATITIS, ACTINODERMATITIS.

A man, aged 32, was first seen in the clinic in 1921, with infectious eczematoid dermatitis of the hands. Various local applications were given and his condition improved. The patient returned home and had a recurrence, for which he received considerable actinotherapy. When he returned here in 1928, extensive skin graft was done, both pedicle grafts and Thiersch grafts, because of the severe burns from the roentgen rays. The patient recently had been working, had been having his hands in water and had been doing heavy lifting, with the result that the dermatitis had recurred. Treatment with foreign protein had failed. He was presented for therapeutic suggestions.

DISCUSSION

DR. SWEITZER: I should recommend packs wet with solution of copper sulphate.

ACNE VULGARIS (PYODERMIA).

A single man, aged 21, reported that since 1923, when his right hip had been fractured, there had been repeated swellings on the extremities and trunk, which had ulcerated and healed, leaving superficial scars. The lesions about the right hip had persisted as draining sinuses and ulcers. The Wassermann reaction of the blood was negative. Roentgenologic examination of the right hip showed evidence of destructive arthritis and ankylosis of the right hip. A culture from the ulcer on the right arm revealed staphylococci and streptococci.

CHRONIC PYODERMIA WITH SERPIGINOUS ULCERATION.

A married woman, aged 48, reported that the onset of her trouble had taken place in 1924. After a slight injury of the left heel, a secondary infection had developed and had spread rapidly. On admission the patient presented multiple discrete and confluent draining abscesses over both legs and feet. The advancing borders were arciform, crusted ulcers, some of which had verrucous bases. Edema, scattered patches of erythema, scarring and crusting involved the rest of both legs. Treatment for syphilis did not improve the condition of the legs. In March, 1929, following an attack of grip, there was a marked flareup of the cutaneous lesions. General examination gave essentially negative results. Scarring from similar lesions was noted on the neck, breast and abdomen.

The laboratory observations were as follows: hemoglobin 55 per cent; slight anisocytosis and poikilocytosis; erythrocytes, 3,870,000 and leukocytes 7,000 in each

cubic millimeter of blood; color index, 0.7 +; differential leukocyte count; lymphocytes 31.5 per cent, neutrophils 63 per cent and eosinophils 0.5 per cent. Repeated blood cultures gave negative results, and cultures from the lesions revealed *Streptococcus hemolyticus*. Roentgenologic examination of the thorax gave negative results. The microscopic picture was that of pyodermia. The patient had been treated with wet dressings of potassium permanganate and Bezredka broth; autogenous vaccine has been given twice a week, ultraviolet light had been given and a high caloric diet had been employed.

Chronic Pyodermia with Serpiginous Ulceration.

A man, aged 33, dated the onset of his trouble from 1920. After a crushing injury to the right leg, gas bacillus infection had resulted and had necessitated amputation below the knee. Ulcers had developed in the stump, and an abscess had been drained. Six months later he had suffered from superficial abrasion of the skin of the left leg. This had not healed so he had been hospitalized, and during this time ulcerating lesions had developed "all over his body." These had cleared up after eighteen weeks. Three months later, the "ulcers" had reappeared, and since then they had been present most of the time. The longest period of freedom had been eight months. He had had lesions continuously for the past two years; they usually had started as flaccid pustules each with an areola of hyperemia. With rupture of the lesions, shallow spreading ulcers had formed. He has a history of recurrent attacks of anorexia, associated with bloody diarrhea. Exacerbation of the cutaneous lesions and rapid loss of weight were noted during the attacks.

The physical examination showed that the man was thin and emaciated and had marked secondary anemia. The heart and lungs were satisfactory. The laboratory observations were as follows: hemoglobin 60 per cent; erythrocytes, on April 8, 1929, 3,890,000, and leukocytes 6,100 in each cubic millimeter of blood; differential count; lymphocytes 29.5 per cent, large mononuclears 1.5 per cent, eosinophils 2 per cent, basophils 0.5 per cent, neutrophils 63 per cent and transitionals 3.5 per cent. There was no growth on blood culture. Delayed growth on cultures from the lesions showed *Streptococcus hemolyticus*. Examination of the stools was negative for parasites or ova. Analysis of the gastric content gave negative results; Wassermann reactions of the blood were negative repeatedly. On June 10, 1929, examination of the blood gave the following results: hemoglobin 70 per cent, erythrocytes 4,740,000 and leukocytes 5,400 in each cubic millimeter; differential count; lymphocytes 40.5 per cent, transitionals 6 per cent, neutrophils 49 per cent and eosinophils 0.3 per cent.

The various biopsies have shown pictures varying from a tuberculoid reaction to subacute pyodermia with numerous abscesses. The patient was given sulphur baths, 2 per cent sulphur in zinc oxide, intravenous typhoid vaccine every four days, pills of ferrous carbonate, ultraviolet light therapy and a high vitamin diet.

Chronic Pyodermia.

A married woman, aged 28, had received a slight injury of the left ankle in October, 1928. The resulting abrasion had developed into a superficial abscess followed by a chronic ulcer which gradually had extended to the dorsum of the foot. In January, 1929, she had noted a "pimple" on her right shoulder which had developed into a small, chronic ulcer, gradually increasing in size. In March, 1929, there had been a "pimple" on the abdomen which had become ulcerated. There had been gradual extension of the superficial ulcer to the size to which it had grown by the time of admission, when it involved the greater part of the skin between the umbilicus and the mons veneris. There were similar, but smaller lesions on the arms, thighs and buttocks. She presented a history of ulcerative colitis, with bloody diarrhea of one and a half years' duration. The general examination showed her to be emaciated and to have marked secondary anemia. The laboratory data were as follows: hemoglobin 55 per cent, erythrocytes 3,550,000 and leukocytes 8,300 in each cubic millimeter of blood; color index, 0.7 +,

lymphocytes 23 per cent, neutrophils, 67 per cent and eosinophils 2 per cent. There was slight anisocytosis, poikilocytosis and polychromatophilia. Blood culture gave no growth. Blood and pus, but no parasites or ova, were found in the stool. The culture from the ulcers demonstrated streptococci and staphylococci. On June 20, 1929, transfusion of 500 cc. of whole blood was given. Biopsy showed essentially a picture of pyodermia, with numerous staphylococci deep in the cutis. The patient was treated with increasing doses, intravenously, of typhoid vaccine and baths of colloid sulphur.

DISCUSSION

DR. MICHELSON: I think that this group of cases is worthy not only of intensive study but of detailed report. There is possibly a common causative factor in the three patients, but the microscopic pictures demonstrate that there is marked variation in the degree of reaction to the infector, representing a definite degree of allergy in each patient. The marked foreign body reaction in the first case of pyodermia is amazing. I should recommend that the work on hospital gangrene by Professor Matzenauer be investigated, for the cases reported by him may be somewhat similar.

DR. BRUNSTING: This group of cases fits in well with those described as chronic ulcerating pyodermia, with serpiginous extension and superficial scar formation, as reported by Ferguson-Smith and Zurhelle and Klein. Others of similar nature have been reported by Cullen, as well as by Engman, dealing with ulcerations of the skin following operation for appendicitis.

DR. SWEITZER: I think, as Dr. Michelson does, that to determine the cause of such infections is important. I saw the second case with Dr. Harry Foerster when the patient showed involvement only of the foot, and it resembled a mycotic reaction. In most of these cases there is an infection with hemolytic streptococci. I saw a similar condition occur after an abdominal operation. A vaccine was made of the organisms and the condition cleared up, later to relapse.

DR. O'LEARY: This group of cases is of particular interest to me because of the underlying diseases that have been demonstrated so frequently in these patients. The laboratory studies have revealed the presence of streptococci and staphylococcic in the ulcers. The bacteriologic studies do not suggest that either organism is etiologic, but that it is the combination of the two comparatively common organisms that have produced digestion of the skin in these patients. The term pyodermia describes the condition. However, the superficial digesting process that is going on in the skin is unique in my experience. The local applications have been futile and the only outstanding therapeutic results have been obtained essentially from treatment with foreign protein. Several years ago, I called attention to the value of treatment with foreign protein in dermatosis, and, at that time, found that chronic infectious diseases in general were those most benefited by this form of treatment. Ulcerative colitis of the type recently described by Bargen, apparently due to streptococci, has been a fairly constant observation in other cases of the same type. There seems to be no affinity between the organisms isolated from the colon and those found in the cutaneous ulcerations. These cases have offered more striking results from intravenous treatment with typhoid vaccine than any of the other forms of dermatosis that we have treated thus far.

DR. MONTGOMERY: The microscopic picture of this group of cases is essentially that of a nonspecific granuloma. In one case in particular, however, there are dense masses of streptococci arranged in coils lying deep in the subcutaneous tissues in the midst of the granulomatous process. The failure to demonstrate any pyogenic organisms in the epidermis and the presence in all cases of staphylococci or streptococci deep in the section would tend to suggest that they were of etiologic significance. Careful search for blastomyces and tubercle bacilli gave negative results in all cases.

EXFOLIATIVE DERMATITIS (ALLERGIC TYPE).

An attorney at law, aged 32, complained of flexural eczema since the age of 4. The condition had been mild for many years, with exacerbations in the winter. He had had a severe attack in 1917, which had lasted all winter. He had joined the army and while in France had been absolutely free from the difficulty. In August, 1919, he had returned home; in November, the dermatitis had returned and had disappeared again in June. In the fall of 1920, he had entered law school in Chicago and for three years had no dermatitis. In July, 1922, he returned to his previous home in Sioux City, and in October had another recurrence. Since then he had some dermatitis practically all the time with flareups in the winter. In 1927, he had undergone appendectomy and tonsillectomy, and had four teeth extracted. After leaving the hospital he had gone to South Dakota. His skin had been clearing rapidly while he was in South Dakota, but he had to leave before it was entirely clear. He returned home in September, and in December had recurrence of the cutaneous lesions. Since then, the dermatitis had been continuous, with an exacerbation each year in June.

There was a history of a similar cutaneous condition in his sister. There was no history of asthma or hay-fever. The general examination and laboratory data were essentially negative. There was generalized adenopathy. The laboratory data were as follows: hemoglobin 75 per cent, erythrocytes 4,710,000 and leukocytes 14,900 in each cubic millimeter of blood; lymphocytes 11 per cent, polymorphonuclears 74 per cent, eosinophils 8 per cent and transitionals 5 per cent. The microscopic picture was that of dermatitis exfoliativa eczematoid in type. A few tiny abscesses were noted in the stratum corneum; these were filled with cocci and not leukocytes.

DISCUSSION

DR. MICHELSON: There is a significant fact in the history that this man gives. It calls to mind the report made by Dr. Butler of the cutaneous conditions found in men in the American Army stationed at American Lake. He said that soldiers who entered the camp with eczema, after a few weeks' stay, without any particular treatment, were usually entirely rid of the disorder.

DR. SWEITZER: I should think that a change of location might benefit a patient with this condition.

INFECTIOUS ECZEMATOID DERMATITIS. SYCOSIS VULGARIS.

In December, 1928, a truck driver, aged 29, reported the onset of a cutaneous condition, with the development of a group of vesicles in the bearded region of the right cheek. They soon became crusted and oozing; later there was pustulation. In January, the lesions spread to his chin, left cheek and eyebrows. The condition was treated with roentgen rays, ultraviolet light and local applications; four teeth were extracted. The lesions continued to spread. They had never involved the upper lip. The general examination and laboratory data gave negative results. Repeated search for trichophytes had been negative. The patient was treated with wet dressings of aluminum acetate, and for his eye, dressings of solution of boric acid and of solution of diacetoxymercuri-4-nitro-2-cresol (1:3,000) three times a day.

DISCUSSION

DR. SWEITZER: This case recalls that of a patient who presented a condition that looked like dermatitis of the face but which developed into sycosis. The patient was hospitalized and cured by means of wet packs and the roentgen ray. The improvement was rapid.

DR. MICHELSON: In addition to the condition of his face, this man has a deep infected fissure at the corner of his mouth. This might be investigated for a possible infection with yeast. Finnerud reported a group of cases of angulus infectiosus that were due to yeast.

LUPUS ERYTHEMATOSUS, DISSEMINATE, SUBACUTE.

A married woman, aged 28, reported that the onset of her condition had been in March, 1927, at the time of childbirth. She had noted fever during puerperium and weakness and malaise thereafter. In September, 1927, there had been "red spots" on her finger tips and palms. Transient swellings that had appeared suddenly and stiffness had become evident at various points. The face had become edematous and the eyelids swollen. In September, she had undergone dilatation and curettage because the menstrual blood was "too pale." In December, 1927, recurrent abdominal attacks characterized by epigastric pain, vomiting and diarrhea had appeared. An attack of this kind had lasted for three or four days and had recurred at intervals of from three weeks to three or four months since. Sometimes before, and always with the attack, urticarial lesions developed on the skin. These lesions appeared suddenly, itched, burned and disappeared suddenly. She had lost weight during the attacks, but had felt well in the intervals between the attacks. She had been able to tell when an attack was coming on by a feeling of stiffness and transient swelling of some joint. Her last attack had been in April, 1929. In May, 1928, there had been a red, scaling lesion of the left malar eminence. It had spread rapidly over the bridge of her nose and right cheek. She had had five treatments with carbon dioxide; the last one had been given in August, 1928. The lesions had spread to the distribution in which they were seen at the time of admission. Pigmentation had developed in September, 1928.

General examination had revealed cervical adenopathy, tenderness in the epigastrium, infected tonsils, graded 2, and periapical infection of the teeth, graded 2. Roentgenographic examination of the thorax, stomach and gallbladder gave negative results. The patient had secondary anemia; hemoglobin was estimated at 35 per cent, erythrocytes numbered 3,000,000 and leukocytes 2,200 in each cubic millimeter of blood; the color index was 0.5 +. Analysis of gastric content revealed total acidity of 40 and free hydrochloric acid of 20 in terms of tenth-normal sodium hydroxide. Biopsy showed a microscopic picture consistent with the clinical diagnosis. The patient was treated with increasing doses of quinine, a high caloric diet and rest in bed.

ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS.

A married woman, aged 22, reported the onset, in September, 1928, of intestinal influenza (?). An erythematous cutaneous lesion had appeared over her nose and cheeks. In October, she had had tonsillitis which had been followed by gradual weakness, drowsiness and pallor. In December, she had noted pain in the right upper quadrant of the abdomen. There had been a gastro-intestinal upset. She had had jaundice of about five months' duration. In May, 1929, the jaundice had practically cleared up. There had been conjunctivitis and dermatitis of the face. She had been treated with ultraviolet light, and the dermatitis subsequently had spread over the face and chest.

Examination disclosed marked secondary anemia, prostration and a temperature of 102 F. There was marked enlargement of the liver and spleen, and both organs were tender on palpation.

Laboratory observations were as follows: hemoglobin 20 per cent, erythrocytes 990,000, platelets 138,000 and leukocytes 7,200 in each cubic millimeter of blood; lymphocytes 27 per cent, neutrophils 65 per cent and transitionals 4.5 per cent. There were marked anisocytosis and moderate polychromatophilia. Blood culture gave negative results. Agglutination for *Bacillus abortus* gave negative results. Biopsy showed a picture consistent with acute lupus erythematosus. There was no evidence of lymphoblastoma. The patient was treated with rest in bed, increasing doses of quinine and a high vitamin diet.

DISCUSSION

DR. GOECKERMAN: In the second case there is evidence of severe toxemia which frequently is associated with acute disseminated lupus erythematosus.

Perhaps it would be better if I said that the cutaneous signs called acute disseminated lupus erythematosus may be part of a severe toxemia, such as is manifested by this patient. This young woman is critically ill, and thus far we have been unable to demonstrate the etiologic factor.

SCLERODERMA (DIFFUSE AND CIRCUMSCRIBED TRAUMATIC ULCER).

A retired farmer, aged 60, reported the onset in January, 1926, of a feeling of roughness and dryness of the skin of his legs and right arm, accompanied by some pruritus. Then the condition had become generalized. There had been increased sensitivity to pain and temperature. He had noted difficulty in movement; his skin had felt "tight." There was no history of exposure to arsenic except such as might have been involved in spraying potatoes the summer before the onset.

General examination gave essentially negative results in April, 1926, except that an enlarged prostate, hemorrhoids and some pyorrhea were found. He had a ruptured choroid and a dislocated retina of the left eye. The blood picture and urinalysis gave negative results, and on May 4, 1926, there was 2 mg. of arsenic in 1,500 cc. of urine. The basal metabolic rate was +5. The Wassermann reaction of the blood was negative, as were roentgenologic studies of the thorax and upper parts of the arms. Studies of capillaries revealed short, undilated capillaries, with an even flow of blood, slightly slowed but without marked disturbances. There was some improvement from treatment with preparations of pituitary gland (anterior lobe) and thyroid gland. Ultraviolet light and warm olive oil massage, also, were administered with some benefit. The patient returned on June 4, 1928, with a traumatic ulcer on the right leg, and he returned again on May 25, 1929, with the same complaint. On June 17, the basal metabolic rate was +1. The test for arsenic in the urine gave negative results.

PITTSBURGH DERMATOLOGICAL SOCIETY

LOUIS WILLARD, M.D., *Secretary*

Regular Meeting, Sept. 16, 1929

HOWARD T. PHILLIPS, M.D., *President*

CARCINOMA ON A GUMMATOUS BASE. Presented by DR. AMSHEL.

I. Y., a man, aged 39, married, was seen for the first time on September 14. He presented a hard, crusted ulceration of two years' duration, with a suggestion of a rolled border involving almost the entire left side of the lower lip. The patient said that he had a chancre about twenty years before presentation and was treated locally. About a month later, he had a generalized rash. A Wassermann reaction taken about a year prior to presentation was negative, but the patient received treatment consisting of two intramuscular injections and six intravenous injections, without any change in the lesion on the lip. A Wassermann reaction taken a week before presentation was also negative. The patient had just received one injection of neoarsphenamine and two injections of bismuth without any change. The cervical glands were not enlarged.

DISCUSSION

DR. HOLLANDER: I agree with the diagnosis and should like to put in a word of warning against any arsenical treatment.

DR. JACOB: I advise wide excision and suturing followed by deep roentgen therapy of the lip and neck.

DR. BUSMAN: I would use the roentgen ray or radium with no surgical measures.

DR. HOLLANDER: First, I think that the infected teeth should be extracted and after the mouth is in good condition gold radium emanation should be implanted all around the lesion and the metastases treated as they arise with radium implants.

DR. PHILLIPS: I think that the roentgen ray should first be used. Then the teeth should be taken care of, and when the entire area is again in a quiescent state, it should be excised. This should be followed by filtered roentgen ray treatment.

LUPUS ERYTHEMATOSUS. Presented by DR. GOLDMANN.

C. V., a white man, aged 31, presented multiple atrophic lesions on the right and left temples and anterior portions of the scalp. The lesions were atrophic and scaly and showed the presence of telangiectasia. The patient first noticed the lesions two months before presentation, but from the extent of the lesions they had been present for a longer period. Physical examination showed the presence of infected tonsils. The chest was normal except for an increase in tactile fremitus over the right upper lobe; there was no moisture. The left lobe of the prostate was somewhat boggy. A smear from the prostate was negative. Gold sodium thiosulphate was being administered.

LUPUS ERYTHEMATOSUS. Presented by DR. HOLLANDER.

Mrs. E. B., aged 47, a housewife, presented on the right cheek two small lesions which were scaly and had an erythematosus base. In addition, there were several areas on the face which were the remnants of previous lesions of this type. The patient had received gold sodium thiosulphate on May 26, 1927. The treatments cleared up this condition. Recurrence began in August, 1929.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. SCHWARTZ and DR. BUSMAN.

C. V., a woman, aged 40, presented discoid lesions over the face and scalp. There were also multiple discreet and confluent papules of the chest, back and forearms. The condition was of three months' duration.

DISCUSSION

DR. CRAWFORD: In dealing with the disseminated type of lupus erythematosus, I advise that the patient be placed in bed for ten days and soothing lotions be applied locally. Then the administration of gold sodium thiosulphate should be begun in doses of from 5 to 10 mg. every five days.

DR. BUSMAN: I do not consider my case one of disseminate lupus erythematosus, as we call the severely toxic type with fatal termination. It is more of an acute generalized lupus erythematosus, and with judicious approach and hospital care, the patient should make an uneventful recovery.

DR. GUY: The localization of most of the lesions in Dr. Busman's case on exposed parts is of interest. Dr. King-Smith called attention to the predisposing effect of ultraviolet light in connection with lupus erythematosus. The rapid extension of lesions of acute disseminated lupus with ultraviolet therapy should constitute a contradiction in this type of case. Dr. Schamberg has treated patients with lupus erythematosus for many months with gold thiosulphate, and he considers it a specific. Frequently the gold compound has to be continued for a long time. Removal of the focal infection certainly is indicated.

DR. HOLLANDER: My reason for bringing my case in was that so few of these patients are being shown, and that there are so few cases of relapse being recorded after treatment with a gold compound. Gold, I believe, is not a specific.

LUPOID SYCOSIS. Presented by DR. HOLLANDER.

C. J., a man, aged 32, married, presented a pyogenic infection affecting the bearded surfaces of the face and eyelashes. Individual pustules pierced by hair could be noted. The extensive scars, where the process had healed, were scale covered and atrophic, and in places (eyelids) contraction had begun. This condition was of four years' standing. On the elbows there was to be noted a dry, scaly condition which, on scratching, showed pinpoint bleeding and resembled psoriasis. Laboratory examinations had been negative. The patient was presented on account of the extreme chronicity and resistance to all types of treatment.

DISCUSSION

DR. GUY: These cases are frequently sources of threatened legal action when, after shopping around for relief, some one inadvisedly suggests that they have been burned with roentgen ray.

DR. CRAWFORD: I suggest treatment of this patient with colloidal manganese.

DR. HOLLANDER: This man has had a great deal of treatment; we have used vigorous injections of a nonspecific milk preparation and then rested, with no effect; gold thiosulphate has been given a generous trial with no reaction and no result; mercuric salicylarsenate did nothing for him and so far auto-inoculation of pus from one of the follicular pustules rubbed into his arm has been of no benefit.

TUBERCULOSIS CUTIS. Presented by DR. HOLLANDER.

Mrs. M. S., aged 42, presented eleven lesions on the face. The lesions were discoid and nodular, and some were covered with a few adherent scales; a definite area of atrophy surrounded the individual lesions. There was no telangiectasia.

This patient had presented herself for examination on Jan. 15, 1929, and since then had received considerable treatment. Twenty-seven injections of gold sodium thiosulphate, of which twelve were full doses, had no effect on these lesions. Removal of infected teeth had no effect. Antisyphilitic treatment was not effective.

On August 8, water-soluble bismuth was given to the patient, and since then there had been a change in the lesions, as evidenced by two lesions on the cheek, in which the pigmentation and nodes were slowly disappearing. An interesting lesion was the largest one over the right side of the lower jaw. It was quite nodular and showed six areas within the lesion in which both the nodules and pigmentation were disappearing.

DISCUSSION

DR. JACOB: I think that this is a condition of syphilis and tuberculosis.

DR. HOLLANDER: Bismuth did good work in this case, and I wonder why the color is increasing while the lesions are apparently improving.

BLACK HAIRY TONGUE. Presented by DR. PHILLIPS.

C. K., a man, a factory worker, aged 50, presented a discoloration on the dorsum of the tongue of about nine months' duration. The central portion was very black while the margins were a yellowish gray. The whole area involved was about 4 by 5 cm. When the long slender filiform projections were removed with a curet the base presented a beefy red appearance, which showed a few oozing points. Repeated applications of a 25 per cent silver nitrate solution to the lesion after thorough curettement had effected no change in its color or character. Subjective symptoms were absent. The patient attributed his trouble to the drinking of "home brew" and "moonshine."

DISCUSSION

DR. GUY: The majority of these patients do very well with the alternate application for five minutes each of a saturated solution of sodium perborate and saturated solution of sodium thiosulphate, with rubbing.

DR. FISHER: I advise the use of the roentgen ray.

DR. HOLLANDER: I advise the use of arsphenamine made cloudy with sodium hydrate, application being made once daily. A solution of arsphenamine is also given the patient for use as a mouth wash. Long continued treatment is necessary, but three patients on whom this treatment was carried out showed good results.

VACCINIA CICATRICES. Presented by DR. CRAWFORD.

A. F., a girl, aged 6, in infancy had a marked vaccinia, involving the cheeks, forehead and forearms, which she had contracted from sisters who had been freshly vaccinated. At that time she had a facial eczema which offered a fertile field to vaccinia. She was presented to show the moderate scarring of the areas which one would have expected to be fairly cicatrized after such a severe involvement.

DISCUSSION

DR. HOLLANDER: I am surprised at the excellent result and should like to know what treatment had been followed.

DR. CRAWFORD: The treatment was application of starch poultices.

BROMODERMA. Presented by DR. WILLARD.

Mrs. V. W., aged 29, a housewife, presented a sharply marginated, round, elevated, granulomatous lesion, 2 inches in diameter, on the outer lower calf of the right leg; the central area was moist and showed numerous fine pustules at the edge; beyond the periphery were two small groups of closely set pustules. The lesion had been lanced twice. She had been taking bromides for epilepsy. The lesion started six weeks before presentation following an injury.

BROOKLYN DERMATOLOGICAL SOCIETY

A. M. PERSKY, M.D., *Secretary*

Sept. 17, 1929

W. H. BEST, M.D., *Presiding*

A CASE FOR DIAGNOSIS (SARCOID?). Presented by DR. ABRAMOWITZ.

Mrs. J. S., aged 49, was born in Russia. She had had no previous illnesses. Two years before presentation, an eruption began on her forehead, spreading to her cheeks. During the month previous to presentation, lesions had appeared on her back. All the lesions were of the same appearance; they varied in size from that of a quarter to that of a half dollar, and were bluish red. The lesions were edematous, infiltrated and slightly scaly. Numerous follicular points were visible in each patch, but no atrophy could be noted. A blood count, Wassermann test and a biopsy had been taken but reports had not been received.

DISCUSSION

DR. WALZER: I am inclined to consider this a case of leukemia. The lesions on the face may possibly suggest sarcoid. From the color of the lesions, I should be inclined to put this case in the group of sarcoids, leukemias, etc., but because of the lesions on the back, which are subcutaneous infiltrated patches, and the superficial lesions on the face, I should favor a diagnosis of leukemia cutis.

DR. CHARGIN: I regard the case as one of fairly typical sarcoid of Boeck. You will recall that Boeck's sarcoids are of three types: small nodular, large nodular and diffuse infiltrations. This patient presents the small nodular variety

on the face and the diffuse infiltrations on the back. The yellowish points to which Boeck calls attention, are beautifully illustrated in this case.

DR. BEST: In the absence of any laboratory data, I do not see what other diagnosis could be made, except a diagnosis of a sarcoid.

NOTE.—The Wassermann reaction was negative. A complete blood count was normal. Examination of the excised lesion showed the histologic structure of a sarcoid of the Spiegler-Fendt type.

URTICARIA PIGMENTOSA (ADULT TYPE). Presented by DR. WALZER.

D. H., a married woman, aged 26, had nothing in her past history of any importance, except that she had been getting progressively more deaf for several years, without any explainable reason.

A skin condition was present which had begun about two and one-half years before presentation, when the patient claimed that the lesions appeared as brown spots which had been increasing in number ever since. Wassermann tests had been made in various clinics and by private physicians, and all had given negative results.

At presentation, numerous brown sharply outlined macules, about the size of a pea, were scattered over the body. When irritated, they became red and somewhat elevated. Pruritus was present, and dermographism was marked.

A CASE FOR DIAGNOSIS (DERMATITIS FACTITIA?). Presented by DR. GAUVAIN.

G. E. R., a married man, a roofer, aged 60, had had a lesion which began ten years before presentation as a small crusted ulcer, which he thought was caused by plucking hairs from his moustache. The lesion continued to increase, until at presentation it involved an area about 1½ inches (3.7 cm.) wide by 2¼ inches (5.6 cm.) long, directed obliquely downward and outward from the right side of the nose to the angle of the mouth. The lesion was a hard fibrous scar, with an indolent ulcer one third as large in the center. The Wassermann reaction of his blood was negative.

Biopsy showed an ulcer of the skin with marked epithelial reaction about its edge and base. Deep in the corium there were several calciform bodies which appeared to have been in the tissues a long time.

The growth was diagnosed as that of a foreign body ulcer of the skin.

DISCUSSION

DR. ABRAMOWITZ: I am inclined to believe that this lesion is self-induced. The lesion shows irregular superficial ulcerations that invade the lip, and it is well known that lesions in this location are not known to last very long before metastases ensue. It may be that the calcification is due to some agent that he is using. It strikes me that the man should be watched very carefully and an occlusive dressing applied, such as starch or plaster of paris. If my diagnosis is correct, his neurosis should be treated by proper measures.

DR. CHARGIN: I do not think that a positive diagnosis can be made without repeated biopsies. I think that the lesion is most likely a basal cell epithelioma.

DR. GRAHAM: I have been watching this case for four or five months. I think Dr. Abramowitz was right when he suggested dermatitis factitia, as we have felt for some time that this was the correct diagnosis. At first we thought it was a malignant growth, but the lesion changes from time to time. At one time, it was nearly healed, the unhealed portion being no larger than a finger-nail. We have never been able to put the patient in a hospital to control him. We have tried to apply dressings, but have never been able to keep them on. It is a hard place to apply a dressing and it may be that that is why it comes off. I am not inclined to think that it is a rodent ulcer.

A CASE FOR DIAGNOSIS (FAVUS?). Presented by DR. SKEER.

S. S., a girl, aged 14, born in the United States, complained of several lesions which began one year before presentation, following trauma, on the vertex of the scalp.

Examination disclosed a patch the size of an orange, on the vertex, consisting of several round areas which were shiny and atrophic in the center. At the periphery were numerous follicular lesions, consisting of a ring of erythema with a yellow crust around the hair follicles.

The first microscopic report from the laboratory came back positive for fungus. The second report was also positive. There were separate mycelial threads in the hairs.

A culture was made, but the report had not been received.

DISCUSSION

DR. WALZER: This case is clinically one of favus.

DR. ABRAMOWITZ: This girl is somewhat above the age for tinea. Clinically, she presents alopecia in one large patch and some smaller patches. There were no broken off hairs. She seems to have some scarring on the scalp, but we have not seen any typical favus cups. The hairs from this girl's scalp, taken from the affected areas, showed long mycelial threads, running throughout the shaft. There were no spores. The mycelial threads showed septate divisions of various lengths. The case is probably one of favus.

ACTINOMYCOSIS. Presented by DR. CHARGIN.

L. G., a girl aged 20, single, a stenographer, consulted a physician two years before presentation for what was regarded as an impacted wisdom tooth on the lower right side. The area was incised to relieve tension. It refused to heal, and a swelling soon developed in the neck. At this time the patient was admitted to a hospital where the condition was diagnosed as Vincent's infection and twelve injections of neoarsphenamine were given. Because of the swelling in the neck actinomycosis was suspected, but the organism was not found. While she was in the hospital, where she remained some weeks, her temperature reached 102 F. In the course of time, the swelling receded and the lesion in the mouth healed. Soon the swellings reappeared. She was then seen elsewhere, where the examination of the smears showed actinomyces. She was given treatment with small doses of potassium iodide and fractional applications of the roentgen rays. Later, she received very large doses of potassium iodide. The condition gradually improved and in the course of time, the patient became practically well but soon relapsed. She was free of all eruption for several months, but later returned with a swelling of the right cheek, the pain being marked over the articulation. Although the cheek was definitely swollen, the skin over the cheek was normal. The area was somewhat tender to the touch. The neck on the right side showed numerous scars of healed lesions and a few small swellings over which was reddened skin. The mucous membrane of the mouth was normal. The patient's general physical state was good.

DISCUSSION

DR. GRAHAM: As I understand it, there have been periods when the potassium iodide was discontinued. In view of the recurrences, it seems to me that a long continuation of this treatment is indicated. It does not seem that more exposure to the roentgen rays is advisable on account of the sequelae already present in the skin.

DR. ABRAMOWITZ: The only suggestion I can make with the exception of surgical intervention, is the use of intravenous injections of Gram's iodine solution, as advocated by Ravaut for tinea sycosis.

DR. WALZER: About one and one-half years ago, I presented the case of a girl about 17 years old with a similar lesion in the same location. She had

received large doses of potassium iodide for a long time and when last seen, she was practically well.

DR. BEST: I suggest that you continue the administration of potassium iodide internally.

DR. CHARGIN: All the roentgen therapy that the patient had received to date was applied below the margin of the jaw, because all her trouble was in the neck. She had persistently been taking iodides in doses of 25 drops. I notice that a success has been obtained in a number of cases with local injections of iodoform, which I would like to use in this case, but am at a loss just where to inject the remedy, since there is no definite area of infiltration or fluctuation.

CLEVELAND DERMATOLOGICAL SOCIETY

H. J. PARKHURST, M.D., *Reporter*

Regular Meeting, Sept. 19, 1929

C. L. CUMMER, M.D., *Presiding*

FOX-FORDYCE DISEASE. Presented by DR. MISKJIAN and DR. HOWARD.

An obese negress, aged 29, had had intense and persistent itching in the axillary and pubic regions ever since she had had scabies, in 1926. The skin in these areas was hyperpigmented and presented many pinhead-sized papules, which were closely grouped but not confluent. There was no axillary hair, but the growth of pubic hair was normal. The histologic observations were characteristic.

KERATOSIS PALMARIS ET PLANTARIS. Presented by DR. LITTMAN.

Several members of a family were presented with the condition, which was said to have been present in three or four succeeding generations.

DISCUSSION

DR. COLE: One of the family showed a little keratosis pilaris about the elbows but no other signs of ichthyosis.

DR. NORRIS: The mother also presented the condition.

DR. COLE: I felt that the mother's condition was not the same, but rather a dryness due to scrubbing and other housework.

PEMPHIGUS OF SENEAR-USHER TYPE. Presented by DR. COLE and DR. DRIVER.

W., a boy, aged 8 years, had previously been presented at several meetings. An eruption of the pemphigus of Senear-Usher type of three and one-half years' duration, had subsided until only the hands, face, feet and genitalia were involved. The bullae, once large and flaccid, had become small and tense. There was no pigmentation. The mucous membranes had not been involved since the initial outbreak. There had been improvement following the institution of each new form of treatment, and recently under treatment with tryparsamid.

PEMPHIGUS. Presented by DR. COLE and DR. DRIVER.

This man had previously been presented before meetings of the society. Six months before presentation he had had a generalized bullous eruption with oral involvement and Nikolsky's sign. This outbreak had faded under the Davis treatment, but a fresh outbreak had followed, after the use of potassium arsenite and finally tryparsamid. The bullae were smaller and more tense, Nikolsky's

sign was absent, there was no oral involvement, and marked pruritus was present. The succeeding outbreaks seemed to be becoming less severe than their predecessors.

DISCUSSION

DR. CUMMER: Has tryparsamid been valuable in such cases?

DR. RAUSCHKOLB: We have seen initial improvement, followed by flareups. We are using it in accordance with Dr. Grindon's suggestions.

DR. COLE: The condition was bad under the Davis treatment, and cleared up under tryparsamid therapy.

DR. FISHER: I have seen patients improve under the Davis treatment and later become worse.

SYPHILIS (CONGENITAL?). Presented by DR. COLE and DR. DRIVER.

M. S., a single woman, aged 56, spoke little English and could give no history. The right side of the skull was irregular and dotted in places with superficial pale scars. This condition had appeared at the age of 16, following a fever thought to have been typhus. At the age of 18 the patient had fallen, injuring her shoulder. Following this event, ulcers had appeared over the back, flanks, shoulders, neck and chest; serpiginous scars remained. One and one-half years before the time of her presentation, swellings had appeared in the left side of the neck; they were excised, and roentgen rays and radium were employed. At that time firm, nonpainful nodules had appeared in each breast and in the lumbosacral region. Seven months before presentation, dusky red irregular serpiginous ulcers had appeared on the upper part of the chest and the anterior side of the neck. Histologic sections from a breast nodule were shown. The Wassermann reaction was strongly positive.

DISCUSSION

DR. DRIVER: It is interesting to note that in the presence of so many cutaneous gummas, over a period of many years, apparently no one had made a diagnosis of syphilis. Although roentgenologic studies of the skull were considered negative, it can be seen that much of the outer table is destroyed.

DR. COLE: The skull condition dates from an attack which may have been typhoid fever; it may have been typhoid osteitis. The cutaneous syphilid is extensive.

TINEA CAPITIS WITH KERION AND LICHENOID TRICHOPHYTID. Presented by DR. COLE and DR. DRIVER.

E. W., a negro boy, aged 6, presented extensive tinea capitis of two months' duration, with much kerion formation and posterior cervical and occipital lymphadenopathy. On the neck and trunk there was a faint eruption of tiny grouped papules, with fine scales, of a month's duration; subjective symptoms were absent. Histologic sections from the back were shown.

EPITHELIOMATOSIS. Presented by DR. COLE and DR. DRIVER.

L. B., a woman, aged 71, presented a small palm-sized, superficially encrusted reddish-brown patch with slightly elevated, infiltrated border, on the left thigh. It was said to have been present for twenty years. There were many other lesions on the trunk, most of which had been treated. Some had apparently healed after applications of solid carbon dioxide. Histologic sections of the lesion on the thigh were presented.

DISCUSSION

DR. CUMMER: I have had a patient with a small cell epithelioma of the face and several elsewhere, including a large fungating basal cell epithelioma of the groin.

DR. DRIVER: This case fits into the group of superficial epitheliomatosis (Montgomery), the patches having the threadlike pearly border. To call these benign precancerous lesions is hardly correct, for they may become basal cell or even prickle cell epitheliomas.

DR. COLE: The treatment is difficult. Radium and roentgen rays often fail. The application of solid carbon dioxide is usually effective, and electrodesiccation is also good. We have had twelve or fifteen such cases since 1914. In almost 50 per cent of the cases this condition has been accompanied by psoriasis. New lesions may continue to develop.

DR. STEINBERG: I have seen four or five such cases, and have secured good results with solid carbon dioxide and with the acid nitrate of mercury.

DR. FISHER: Has there been any history of arsenical medication in psoriatic patients with epitheliomatosis?

DR. COLE: No such inquiry was made in our cases, but no arsenical keratoses were observed.

ALLERGIC DERMATITIS. Presented by DR. LEVINE.

I. L. C., a boy, aged 15, had been considerably incapacitated since infancy by frequent and more or less generalized outbreaks of dermatitis. A recent extensive flareup had faded completely after the exclusion of egg, milk and wheat from the diet. The eruption had reappeared following the ingestion of rice.

URTICARIA PIGMENTOSA. Presented by DR. RAUSCHKOLB.

M. R., a girl, aged 2½ years, presented a widespread eruption of brown macules, varying in size from that of a pea to that of a small coin which became red wheals when rubbed, and were located on all parts excepting the face. It had been present since the age of 4 months.

A CASE FOR DIAGNOSIS. Presented by DR. FISHER.

Mrs. F., aged 45, said that a small patch had appeared on the right side of her lower lip two and one-half months previously, following a "cold sore." This patch had gradually enlarged, and under observation a second patch had appeared adjacent to the first, no vesicles having been seen.

DISCUSSION

DR. COLE: I should consider this a case of localized cheilitis following repeated herpetic outbreaks.

RADIODERMATITIS FOLLOWING EPILATION BY TRICHO METHOD. Presented by DR. COLE and DR. DRIVER.

A man had had an extensive growth of hair removed from his body at the Tricho Institute in 1923 and 1924. There was extensive atrophy and telangiectasia of the treated areas, especially the trunk.

DISCUSSION

DR. COLE: At the last meeting of the American Medical Association, resolutions were passed requesting reports of such cases seen.

Book Reviews

MALADIES DU CUIR CHEVELU: V. LES SYNDROMES ALOPÉCIQUES, PÉLADES ET ALOPÉCIES EN AIRES. By DR. R. SABOURAUD. Paris: Masson & Cie.

This book is the fifth volume of Sabouraud's extensive work on diseases of the scalp, the first concerning itself with seborrhea, the second with pityriasis of the scalp, the third with the tineas and the fourth with pyogenic infection. The work comprises 345 pages of text and a most extensive bibliography. There are twenty-nine chapters, which are divided into five distinct parts. The first part embraces the clinical study of the various forms of areate alopecia and consists of eight chapters. The second portion, consisting of four chapters, is concerned with the minute microscopic anatomy of the hair and the scalp in the various forms of areate alopecia, together with differential diagnostic features. The third part embraces four chapters, and is a thorough study of the concomitant morbid processes and the influence of heredity which are found in occasional cases of alopecia areata. The association of psoriasis, vitiligo and alopecia areata is discussed at great length. The association of hereditary and acquired syphilis occupies an entire chapter, as do malnutrition and tuberculosis.

The fourth part of the volume, containing four chapters, embraces the discussion of provocative causes such as contagion, alopecia areata occurring following infection, trauma and emotional shock. The final portion of the book takes up in nine chapters the investigative problems concerning the endocrine origin and the association of the sympathetic nervous system to the development of alopecia areata. Herein may be found extensively discussed the question of sex and age, alopecia areata and the menopause, eunuchism and thyroid dysfunction. Two chapters take up in detail the sympathetic origin of Jacquets. One chapter is devoted to basal metabolism and its relation to alopecia.

The volume is written in the easy manner that is characteristic of Sabouraud. It is devoid of colloquialism, and is easy reading for one familiar with ordinary French. The illustrations, which are numerous, are excellent, as are the photomicrographic reproductions. The volume is a fitting monument to the author's extraordinary and profound knowledge of the subject, which has given him a unique place in dermatologic science. It is a volume that should occupy a place in every dermatologist's library.

Directory of Dermatologic Societies *

NATIONAL DERMATOLOGIC SOCIETIES

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

William H. Guy, Chairman, Jenkins Arcade, Pittsburgh.
Francis E. Senear, Secretary, 55 E. Washington St., Chicago.
Place: Detroit. Time: June 23-27, 1930.

American Dermatological Association

Udo J. Wile, President, University Hospital, Ann Arbor, Mich.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: Cleveland. Time: 1930.

British Association of Dermatology and Syphilology (Canadian Branch)

Gustave Archambault, President, 544 East Sherbrooke, St., Montreal.
Albéric Marin, Secretary, 544 East Sherbrooke St., Montreal.

SECTIONAL DERMATOLOGIC SOCIETIES

Baltimore and Washington Dermatological Society

Frank J. Eichenlaub, President, 1835 Eye St., N. W., Washington, D. C.
Leon Ginsburg, Secretary, 1800 N. Charles St., Baltimore.

Iowa and Western Illinois Dermatological Association

Robert E. Jameson, President, 1015 First National Bank Bldg., Davenport, Iowa.
A. T. Leipold, Secretary, 1419½ 5th Ave., Moline, Ill.

New England Dermatological Society

Walter T. Garfield, President, 19 Bay State Rd., Boston.
Rudolph Jacoby, Secretary, 270 Commonwealth Ave., Boston.

Southern Medical Association, Section on Dermatology

Jeffrey C. Michael, Chairman, 1017 Medical Arts Bldg., Houston, Texas.
Emmet R. Hall, Secretary, Exchange Bldg., Memphis, Tenn.

STATE DERMATOLOGIC SOCIETIES

Louisiana Dermatological Society

M. T. Van Studdiford, Pere Marquette Bldg., New Orleans.
Thomas A. Maxwell, Secretary-Treasurer, 1119 Union Indemnity Bldg., New Orleans.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Walter J. Highman, Chairman, 853 7th Ave., New York.
Albert R. McFarland, Secretary, 348 University Ave., Rochester.

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* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON DERMATOLOGY

Frank E. Knowles, 2035 Spruce St., Pittsburgh.
Sigmund S. Greenbaum, Secretary, 1714 Pine St., Philadelphia.

MINNESOTA DERMATOLOGICAL SOCIETY

Edward C. Gager, President, 350 St. Peter St., St. Paul.
D. D. Turnacliff, Secretary, Yeates Bldg., Minneapolis.

OKLAHOMA DERMATOLOGICAL ASSOCIATION

M. M. Roland, President, 117 N. Broadway, Oklahoma City.
W. A. Showman, Secretary, 108 W. 6th St., Tulsa.

LOCAL DERMATOLOGIC SOCIETIES

ATLANTA DERMATOLOGICAL SOCIETY

Howard Hailey, President, Candler Bldg., Atlanta, Ga.
H. S. Alden, Secretary, Medical Arts Bldg., Atlanta, Ga.

BRONX DERMATOLOGICAL SOCIETY

George Spinner, Chairman, 811 Cauldwell Ave., Bronx, N. Y.
Ralph Breakstone, Secretary-Treasurer, 783 Beck St., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

E. Almore Gauvain, President, 47 Halsey St., Brooklyn.
A. M. Persky, Secretary, 1750 Ocean Pkwy., Brooklyn.

CHICAGO DERMATOLOGICAL SOCIETY

Harry R. Foerster, President, Colby-Abbott Bldg., Milwaukee.
E. A. Oliver, Secretary, 55 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

James Miller, President, Berkshire Bldg., Cincinnati.
R. R. Du Casse, Secretary-Treasurer, 19 W. 7th St., Cincinnati.

CLEVELAND DERMATOLOGICAL SOCIETY

Clyde L. Cummer, President, 2417 Prospect Ave., Cleveland.
Robert E. Barney, Secretary, Osborn Bldg., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

Arthur E. Schiller, President, 10 Peterboro St., Detroit.
William G. Schlegelmilch, Secretary-Treasurer, 7769 Grand River, Detroit.

LOS ANGELES COUNTY MEDICAL ASSOCIATION, DERMATOLOGIC SECTION

George F. Koetter, Chairman, 1136 W. 6th St., Los Angeles.
H. Sutherland-Campbell, Secretary, 1936 Wilshire Blvd., Los Angeles.

MANHATTAN DERMATOLOGICAL SOCIETY

David L. Satenstein, Chairman, 57 W. 57th St., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

John Frank Fraser, Chairman, 100 W. 59th St., New York.
Max Scheer, Secretary, 3 E. 53d St., New York.

NEW YORK DERMATOLOGICAL SOCIETY

Paul E. Bechet, President, 30 E. 40th St., New York.
J. Frank Fraser, Secretary, 100 W. 59th St., New York.

PHILADELPHIA DERMATOLOGICAL SOCIETY

A. Strauss, President, 1601 Walnut St., Philadelphia.
Carroll S. Wright, Secretary, 1402 Spruce St., Philadelphia.

PITTSBURGH DERMATOLOGICAL SOCIETY

Howard T. Phillips, Chairman, National Exchange Bank Bldg., Wheeling, W. Va.
Louis Willard, Secretary, 328 Jenkins Bldg., Pittsburgh.

ST. LOUIS DERMATOLOGICAL SOCIETY

Robert H. Davis, President, Missouri Bldg., St. Louis.
Norman Tobias, Secretary, Missouri Bldg., St. Louis.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Thomas Clarke, Madison-Lake Apts., Oakland, Calif.
H. J. Templeton, Secretary, 3115 Webster St., Oakland, Calif.

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